DUR Board Meeting
June 5, 2019
Brynhild Haugland Room

North Dakota Medicaid
DUR Board Meeting Agenda
Brynhild Haugland Room
State Capitol
600 East Boulevard Avenue
Bismarck, ND
June 5, 2019
1:00 pm

1. Administrative items
    - Travel vouchers

2. Old business
    - Review and approval of 04/2019 meeting minutes
    - Budget update
    - Legislative Update
    - Review top 15 therapeutic categories/top 25 drugs
    - Prior authorization/PDL update
    - Second review of Sivextro
    - Second review of Nuzyra
    - Second review of estrogen agents
    - Second review of agents for treatment of osteoporosis
    - Second review of agents for treatment of hyperkalemia
    - Second review of agents for treatment of Parkinson's disease

3. New business
    - Review of short-acting opioid analgesic agents
    - Review of agents for the treatment of thrombocytopenia
    - Review of agents for the treatment of interstitial cystitis
    - Review of agents for the treatment of narcolepsy
    - Report on utilization data from select drugs and drug classes
    - Retrospective DUR criteria recommendations

    - Upcoming meeting date/agenda.
        - Next meeting is September 4, 2019 in the Brynhild Haugland Room

4. Adjourn

Please remember to silence all cellular phones during the meeting.

Drug Utilization Review (DUR) Meeting Minutes
April 9, 2019

Members Present: Michael Booth, Gabriela Balf, Tanya Schmidt, Andrea Honeyman, Peter Woodrow, Jesse Rue, Katie Kram, LeNeika Roehrich, Kayli Bardell

Members Absent: Michael Quast, Jeffrey Hostetter, Russ Sobotta, Laura Schield

Medicaid Pharmacy Department: Brendan Joyce, Alexi Murphy

Old Business

Chair L. Roehrich called the meeting to order at 1:07 p.m. Chair L. Roehrich asked for a motion to approve the minutes of the December meeting. P. Woodrow moved that the minutes be approved and K. Kram seconded the motion. Chair L. Roehrich called for a voice vote to approve the minutes. The motion passed with no audible dissent.

Review Top 15 Therapeutic Categories/Top 25 Drugs

B. Joyce presented the quarterly review of the top 15 therapeutic classes by total cost of claims, top 25 drugs based on number of claims, and top 25 drugs based on claims cost for the 4th quarter of 2018.

PDL/PA Criteria Updates

A. Murphy shared with the Board all of changes made to the Preferred Drug List since the most recent version of the Preferred Drug List was posted. Notable changes included removing PA requirements from 7 ACE/ARB containing agents, as well as from QVAR RediHaler, Relistor syringe, Spiriva Respimat, Striverdi Respimat, and trospium. Other notable changes including adding the following agents to PA: colchicine, Dupixent, Emgality, Novolin 70-30 Flexpen, Nystatin-Triamcinolone, Omnaris, Pataday, and Tracleer. When a new version of the PDL is published and posted to the website, all updates/changes made since the last version are called out at the top of the document itself.

Second Review of Orilissa

A motion and second was made at the December meeting to place Orilissa on prior authorization. The topics were brought up for a second review. A. Murphy explained to the board that examples of specific agents would be added to the form for the sake of clarity. Margaret Olman of AbbVie offered to provide the Board with any information they would like regarding Orilissa. Chair L. Roehrich called for a voice vote to approve the presented criteria, and the motion passed with no audible dissent.

Second Review of Vaginal Anti-Infective Agents

A motion and second was made at the December meeting to generate prior authorization criteria for vaginal anti-infective agents. The topic was brought up for a second review. A. Murphy proposed that the Board remove the 30-day requirement listed in the criteria. J. Rue motioned to amend the criteria as suggested and P. Woodrow seconded the motion. There was no public comment. Chair L. Roehrich called for a voice vote on the amended criteria, and the motion passed with no audible dissent.

Second Review of Agents for the Treatment of Glaucoma
A motion and second was made at the December meeting to place agents for the treatment of glaucoma on prior authorization. The topic was brought up for a second review. There was no public comment. Chair L. Roehrich called for a voice vote and the motion passed with no audible dissent.

Second Review of Agents for the Treatment of Dry Eye Syndrome
A motion and second was made at the December meeting to place agents for the treatment of dry eye syndrome on prior authorization. The topic was brought up for a second review. There was no public comment. Chair L. Roehrich called for a voice vote and the motion passed with no audible dissent.

New Business

Review of Estrogen Agents
A. Murphy presented a review of estrogen agents to the Board. A motion was made by J. Rue to create a new PA criteria class and manage these medications through prior authorization. The motion was seconded by K. Kram. This topic will be reviewed at the next meeting.

Review of Sivextro
A. Murphy presented a review of Sivextro to the Board. A motion was made by K. Kram to create PA criteria for the use of this agent and manage this medication through prior authorization. The motion was seconded by A. Honeyman. This topic will be reviewed at the next meeting.

Review of Nuzyra
A. Murphy presented a review of Nuzyra to the Board. A motion was made by P. Woodrow to create PA criteria for the use of this agent and manage this medication through prior authorization. The motion was seconded by K. Kram. This topic will be reviewed at the next meeting.

Agents for Treatment of Osteoporosis
A. Murphy presented a review of agents for treatment of osteoporosis to the Board. A motion was made by J. Rue to create a new PA criteria class and manage these medications through prior authorization. The motion was seconded by K. Kram. This topic will be reviewed at the next meeting.

Agents for Treatment of Hyperkalemia
A. Murphy presented a review of agents for treatment of hyperkalemia to the Board. A motion was made by J. Rue to create a new PA criteria class and manage these medications through prior authorization. The motion was seconded by A. Honeyman. This topic will be reviewed at the next meeting.

Agents for Treatment of Parkinson's Disease
A. Murphy presented a review of agents for treatment of Parkinson's disease to the Board. A motion was made by M. Booth to create a new PA criteria class and manage these medications through prior authorization. The motion was seconded by J. Rue. This topic will be reviewed at the next meeting.

Report on Utilization of Long-Acting Beta Agonist/Inhaled Corticosteroid Inhaler Combination Products Without Use of a Rescue Inhaler

In 2018, a claims processing edit was put in place requiring that patients receiving a long-acting beta agonist/inhaled corticosteroid (LABA/ICS) combination inhaler must also have a paid claim for a rescue inhaler within the past year to ensure the patient has access to a rescue inhaler. To evaluate the effect of this edit, T. DeRuiter presented utilization data showing the number of FFS patients receiving a (LABA/ICS) combination inhaler without having a paid claim for a rescue inhaler within the past year, comparing the number of patients before and after the claims processing edit was put in place. The data showed that only 5 patients are currently receiving a LABA/ICA inhaler without also having paid claims for a rescue inhaler, as compared to 49 patients prior to the edit being put in place.

Report on Utilization of Guideline Supported Use of Metformin

To promote appropriate, guideline supported use of metformin as a first-line agent for patients with diabetes mellitus type 2, a claims processing edit was put in place on preferred DPP-4 inhibitor, GLP-1 agonist, or SGLT-2 inhibitors. The edit requires that, for claims of these preferred agents to pay automatically at the point of sale and not require PA approval, the patient must be currently stable on a metformin-containing agent with good compliance over the past 3 months. To evaluate the impact of this edit, T. DeRuiter presented utilization data showing the number of FFS patients receiving one of these agents without concomitant use of a metformin-containing agent, comparing the number of patients before and after the claims processing edit was put in place. The data showed a reduction in the number of patients receiving one of these agents without metformin for all of these agents with the exception of linagliptin, resulting in 53 fewer patients receiving these medications without using metformin.

Retrospective Drug Utilization Review (RDUR) Criteria Recommendations

The recommended RDUR criteria enclosed in the packet were developed from product information provided by the manufacturers and are usually consistent with new indications, new drugs added, and new warnings. These proposed criteria will be added to the current set of criteria and will be used in future DUR cycles. J. Rue moved to amend the new criteria as stated above and approve it. K. Kram seconded the motion. The motion passed with no audible dissent.

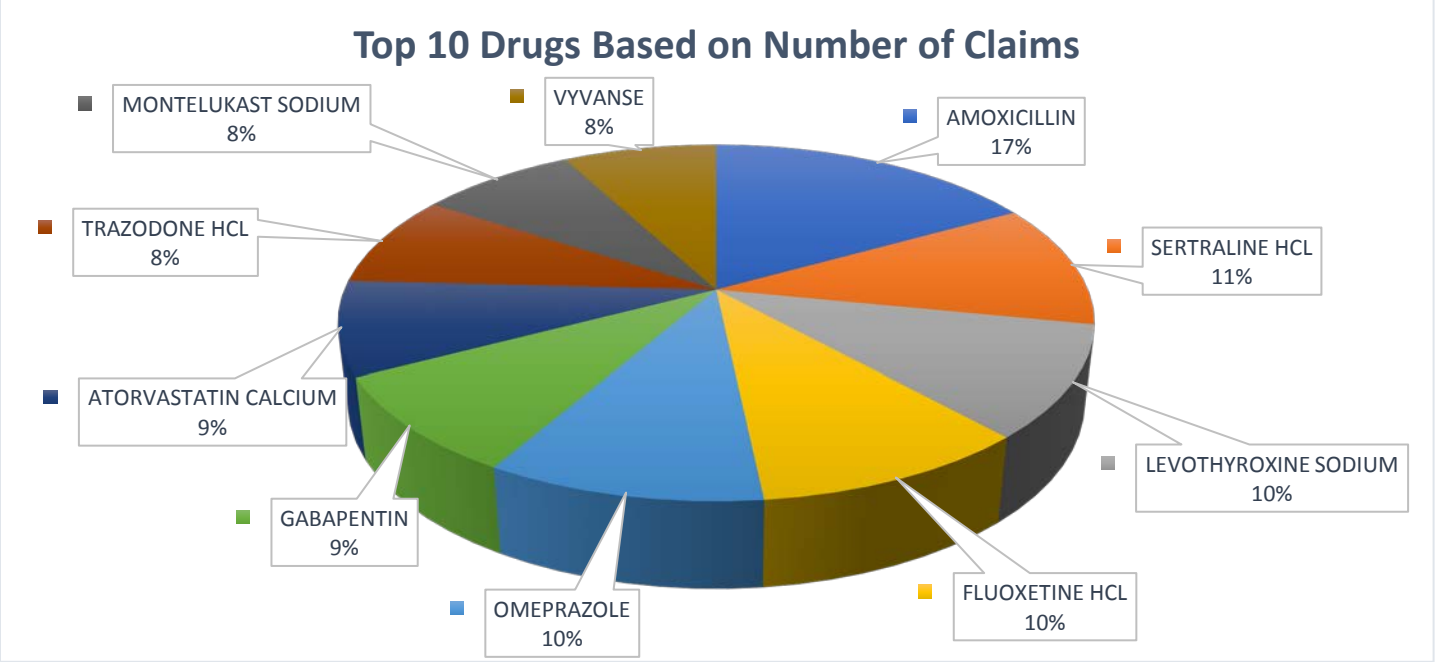
Adjournment and Upcoming Meeting Date

Chair L. Roehrich adjourned the meeting at 2:20 pm. The next DUR Board meeting will be held June 5, 2019 at 1:00 pm at the State Capitol building in the Brynhild -Haugland room.

TOP 25 DRUGS BASED ON NUMBER OF CLAIMS FROM 01/01/2019 – 03/31/2019

Drug	AHFS Class	Claims	Claims Cost	Total Patients	Cost Per Claim	% Total Claims
AMOXICILLIN	PENICILLIN ANTIBIOTICS	4,009	$160,026.16	3,708	$39.92	2.70%
SERTRALINE	ANTIDEPRESSANTS	2,664	$61,741.84	1,202	$23.18	1.79%
LEVOTHYROXINE	THYROID AGENTS	2,402	$45,552.31	879	$18.96	1.62%
FLUOXETINE	ANTIDEPRESSANTS	2,391	$43,817.77	1,040	$18.33	1.61%
OMEPRAZOLE	PROTON-PUMP INHIBITORS	2,383	$44,870.84	1,124	$18.83	1.61%
GABAPENTIN	ANTICONVULSANTS, MISC	2,122	$40,017.54	895	$18.86	1.43%
ATORVASTATIN	HMG-COA INHIBITORS	2,023	$54,138.14	816	$26.76	1.36%
TRAZODONE	ANTIDEPRESSANTS	1,980	$33,048.50	864	$16.69	1.33%
MONTELUKAST	LEUKOTRIENE MODIFIERS	1,895	$36,742.23	938	$19.39	1.28%
VYVANSE	AMPHETAMINES	1,861	$419,470.94	720	$225.40	1.25%
LISINOPRIL	ACE INHIBITORS	1,833	$47,685.41	786	$26.01	1.23%
ESCITALOPRAM	ANTIDEPRESSANTS	1,755	$37,910.34	833	$21.60	1.18%
CLONIDINE	CENTRAL ALPHA-AGONISTS	1,626	$30,701.73	673	$18.88	1.10%
HYDROCODONE-APAP	OPIATE AGONISTS	1,593	$37,122.43	1,018	$23.30	1.07%
AMOXICILLIN-CLAVULANATE	PENICILLIN ANTIBIOTICS	1,548	$80,186.54	1,432	$51.80	1.04%
AZITHROMYCIN	MACROLIDE ANTIBIOTICS	1,547	$46,497.95	1,418	$30.06	1.04%
PROAIR HFA	BETA-ADRENERGIC AGONISTS	1,526	$118,343.75	1,506	$77.55	1.03%
METFORMIN	BIGUANIDES	1,487	$27,112.99	647	$18.23	1.00%
CONCERTA	CNS STIMULANTS	1,462	$464,554.61	599	$317.75	0.99%
RISPERIDONE	ANTIPSYCHOTIC AGENTS	1,453	$21,004.15	479	$14.46	0.98%
LAMOTRIGINE	ANTICONVULSANTS, MISC	1,371	$24,195.97	470	$17.65	0.92%
DULOXETINE	ANTIDEPRESSANTS	1,356	$33,716.49	518	$24.86	0.91%
ARIPIPRAZOLE	ANTIPSYCHOTIC AGENTS	1,306	$30,991.98	516	$23.73	0.88%
ALBUTEROL	BETA-ADRENERGIC AGONISTS	1,290	$54,308.74	1,042	$42.10	0.87%
ASPIRIN	NSAIDS	1,289	$64,481.90	515	$50.02	0.87%

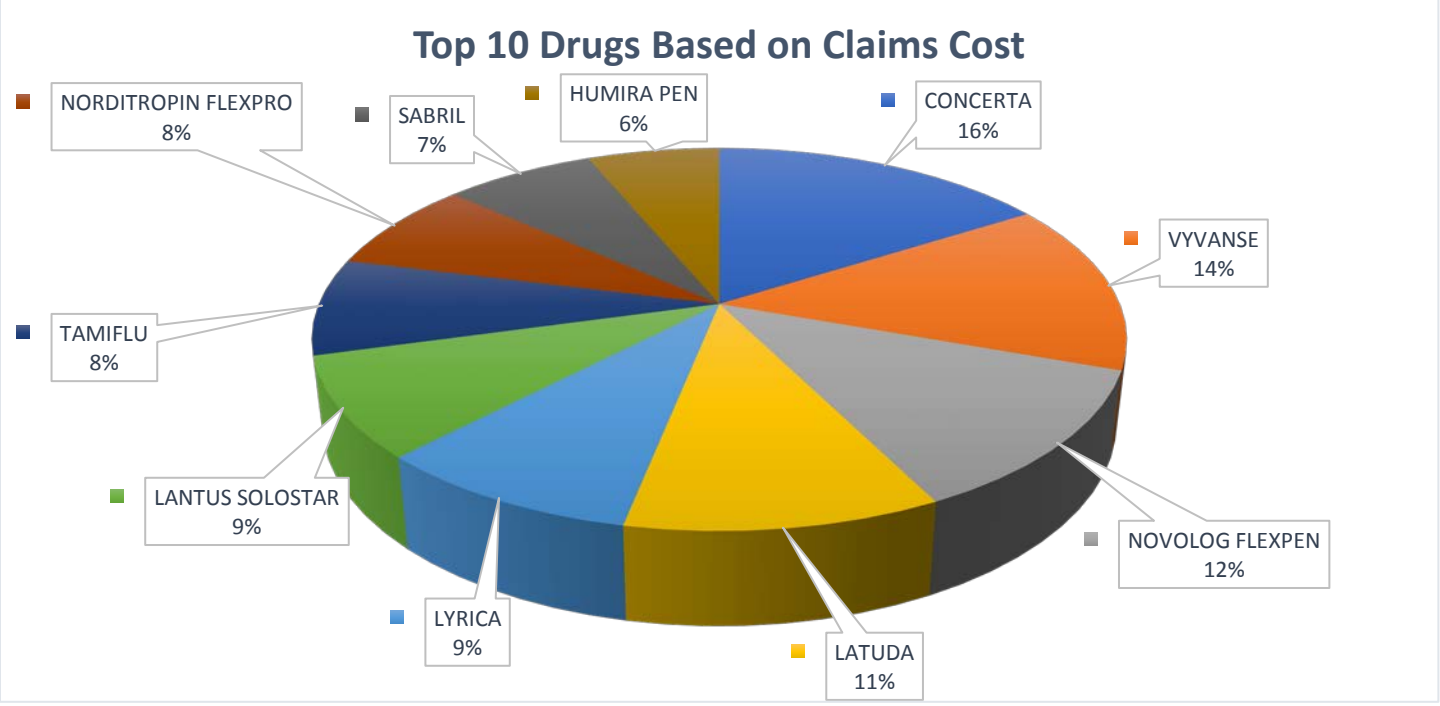
Total Rx Claims From 01/01/2019 – 03/31/2019	148,423



TOP 25 DRUGS BASED ON TOTAL CLAIMS COST FROM 01/01/2019 – 03/31/2019

Drug	AHFS Class	Claims Cost	Claims	Total Patients	Cost Per Claim	% Total Cost
CONCERTA	CNS STIMULANTS	$464,554.61	1,462	599	$775.55	3.61%
VYVANSE	AMPHETAMINES	$419,470.94	1,861	720	$582.60	3.26%
NOVOLOG FLEXPEN	INSULINS	$349,800.28	611	338	$1,034.91	2.72%
LATUDA	ANTIPSYCHOTIC AGENTS	$307,028.31	461	163	$1,883.61	2.39%
LYRICA	ANTICONVULSANTS, MISC	$262,553.24	534	212	$1,238.46	2.04%
LANTUS SOLOSTAR	INSULINS	$246,641.39	564	284	$868.46	1.92%
TAMIFLU	NEURAMINIDASE INHIBITOR	$237,668.85	1,244	1,224	$194.17	1.85%
NORDITROPIN FLEXPRO	PITUITARY	$222,580.85	68	30	$7,419.36	1.73%
SABRIL	ANTICONVULSANTS, MISC	$207,099.76	15	6	$34,516.63	1.61%
HUMIRA PEN	IMMUNOMODULATORS	$181,758.59	34	17	$10,691.68	1.41%
INVEGA SUSTENNA	ANTIPSYCHOTIC AGENTS	$172,005.99	84	31	$5,548.58	1.34%
GENVOYA	ANTIRETROVIRALS	$167,119.03	134	59	$2,832.53	1.30%
AMOXICILLIN	PENICILLIN ANTIBIOTICS	$160,026.16	4,009	3,708	$43.16	1.24%
VIMPAT	ANTICONVULSANTS, MISC	$138,117.38	212	61	$2,264.22	1.07%
LEVEMIR FLEXTOUCH	INSULINS	$132,797.15	309	180	$737.76	1.03%
ADVAIR DISKUS	ICS	$129,051.88	343	191	$675.66	1.00%
LICE KILLING	SCABICIDES & PEDICULICIDES	$121,940.00	276	206	$591.94	0.95%
PROAIR HFA	BETA-ADRENERGIC AGONISTS	$118,343.75	1,526	1,506	$78.58	0.92%
FLOVENT HFA	ICS	$113,178.49	510	330	$342.97	0.88%
MAPAP	ANALGESICS, MISC.	$113,098.38	489	356	$317.69	0.88%
FOCALIN XR	CNS STIMULANTS	$108,838.00	326	129	$843.71	0.85%
SYMBICORT	ICS	$95,692.10	309	177	$540.63	0.74%
TRIUMEQ	ANTIRETROVIRALS	$93,578.56	61	28	$3,342.09	0.73%
NIX	SCABICIDES & PEDICULICIDES	$92,920.62	217	193	$481.45	0.72%
ZUBSOLV	OPIATE PARTIAL AGONISTS	$88,909.41	512	95	$935.89	0.69%

Total Claims Cost From 01/01/2019 – 03/31/2019	$12,869,942.46



PDL Update

ADDED TO PA	
ARNUITY ELLIPTA 100 MCG INH	Inhaled Corticosteroids
BETAXOLOL HCL	Ophthalmic Glaucoma - Beta Blockers
BIMATOPROST	Ophthalmic Glaucoma - Prostaglandin
BRIMONIDINE TARTRATE	Ophthalmic Glaucoma - Alpha Adrenergic
CLINDAMYCIN PHOSPHATE	Vaginal Anti-infectives
DEXAMETHASONE 0.1% EYE DROP	Ophthalmic Anti-Inflammatory
DICLOFENAC SOD EC 50 MG TAB	NSAIDS
DONEPEZIL 23mg	Antidementia
DUOBRII 0.01%-0.045% LOTION	Antipsoriatics - Topical
DUREZOL	Ophthalmic Anti-Inflammatory
ENVARSUS XR	Preferred Dosage Forms
ESOMEP-EZS	Proton Pump Inhibitor
GATTEX	Meds over $3000/month
GYNAZOLE 1	Vaginal Anti-infectives
HALOBETASOL PROPIONATE	Corticosteroids - Topical
INGREZZA INITIATION PACK	Tardive Dyskinesia
INVELTYS	Ophthalmic Anti-Inflammatory
LOTEMAX SM	Ophthalmic Anti-Inflammatory
MAVENCLAD	Multiple Sclerosis - Oral Non-Interferons
MAYZENT	Multiple Sclerosis - Oral Non-Interferons
METRONIDAZOLE	Vaginal Anti-infectives
MICONAZOLE 3	Vaginal Anti-infectives
NORGESIC FORTE	Skeletal Muscle Relaxants
OXERVATE	Meds over $3000/month
QMIIZ ODT	NSAIDS
ROCKLATAN	Ophthalmic Glaucoma - Other
SKYRIZI	Cytokine Modulators
TAKHZYRO	Hereditary Angioedema
TERCONAZOLE	Vaginal Anti-infectives
TESTOPEL	Androgens
TIMOLOL MALEATE	Ophthalmic Glaucoma - Beta Blockers
TIROSINT	Preferred Dosage Forms
TIROSINT-SOL	Preferred Dosage Forms
TREMFYA	Cytokine Modulators
VYZULTA	Ophthalmic Glaucoma - Prostaglandin
XELPROS	Ophthalmic Glaucoma - Prostaglandin

Removed from PA	
ARCAPTA NEOHALER	COPD-Long Acting Beta Agonists
INCRUSE ELLIPTA	COPD-Long Acting Anticholinergics
MENTAX	Antifungals - Topical
SEEBRI NEOHALER	COPD-Long Acting Anticholinergics
TOLTERODINE TARTRATE ER	Unirnary Antispasmodics

Antibiotics - Resistance Prevention

Approval Duration:
Initial: 5 days
Renewal: 5 days

Initial Criteria:

- Patient must be of an appropriate age for use per manufacturer label
- Patient must have an FDA approved indication for use, proven to be caused by a susceptible microorganism by culture and susceptibility testing
- Medication must be prescribed by, or in consultation with, an infection disease specialist.
- One of the following criteria must be met:
  - Prescriber must provide evidence-based medical justification for use, explaining why a preferred antibiotic is not an option due to susceptibility, previous failed trials, or other contraindications (subject to clinical review)
  - Patient is continuing treatment upon discharge from an acute care facility

Renewal Criteria:

- Prescriber must attest that the patient's condition is improving and that it is medically necessary to continue treatment course after re-evaluation of the patient's condition.
- The total requested duration of use must not be greater than manufacturer labeling or treatment guideline recommendations (whichever is greater).

Methicillin-Resistant *Staphylococcus aureus* (MRSA):

Preferred	Non-Preferred
Clindamycin	BAXDELA (Delafloxacin)
Doxycycline	NUZYRA (Omadacycline)
Linezolid	SIVEXTRO (Tedizolid)
Minocycline	
Trimethoprim-Sulfamethoxazole	

health information designs

Antibiotics – Resistance Prevention Prior Authorization Form

Fax Completed Form to: 855-207-0250
For questions regarding this Prior authorization, call 866-773-0695

Prior Authorization Vendor for ND

ND Medicaid requires that patients receiving a prescription for select antibiotics to meet the following criteria:

- Medication must be prescribed by, or in consultation with, an infection disease specialist
- Patient must be of an appropriate age for use per manufacturer label and have a diagnosis of an FDA approved indication for use, proven to be caused by a susceptible microorganism by culture and susceptibility testing
- One of the following must be met:
  - Prescriber must provide evidence-based medical justification for use, explaining why a preferred antibiotic is not an option due to susceptibility, previous failed trials, or other contraindications (subject to clinical review)
  - Patient is continuing treatment upon discharge from an acute care facility

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name	Specialist involved in therapy (if not treating physician)		
Prescriber NPI	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage:	**Diagnosis for this request:**		

Qualifications for coverage:

Has the provider attached documentation showing that the patient's infection is caused by a susceptible microorganism by culture and susceptibility testing?	□ YES □NO
Is the patient continuing treatment upon discharge from an acute care facility?	□ YES □NO
RENEWAL ONLY: Is the patient's condition improving and continued treatment is required after re-evaluation of their condition?	□ YES □NO

Justification for use over preferred agents (provide below or in documentation attached to this request):

□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*

Prescriber (or Staff) / Pharmacy Signature**	Date

**: *By completing this form, I hereby certify that the above request is true, accurate and complete. That the request is medically necessary, does not exceed the medical needs of the member, and is clinically supported in the patient's medical records. I also understand that any misrepresentations or concealment of any information requested in the prior authorization request may subject me to audit and recoupment.*

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Estrogens

Criteria:

- Patient must have failed 30-day trials of at least two preferred products, as evidenced by paid claims or pharmacy printouts.

Preferred	Non-Preferred
CLIMARA PRO (estradiol-levonorgestrel) PATCH	Estradiol patch
COMBIPATCH (Estradiol- Norethindrone)	Estradiol vaginal cream
DIVIGEL (estradiol) GEL	Estradiol vaginal tablet
ELESTRIN (estradiol) GEL	FEMRING (estradiol)
Estradiol- Norethindrone tablet	MINOSTAR (estradiol) PATCH
Estradiol tablet	PREFEST (estradiol-norgestimate) TABLET
ESTRING (estradiol)	
EVAMIST (estradiol) SPRAY	
MENEST (estrogens, esterified) TABLET	
Norethindrone-Ethinyl Estradiol tablet	
PREMARIN (estrogens, conjugated) TABLET	
PREMARIN (estrogens, conjugated) VAGINAL CREAM	
PREMPHASE (estrogen, conj.,m-progest) TABLET	
PREMPRO (estrogen, conj.,m-progest) TABLET	
VAGIFEM (estradiol) VAGINAL TABLET	
YUVAFEM (estradiol) VAGINAL TABLET	

health information designs

General
Prior Authorization Form

Fax Completed Form to:
855-207-0250
For questions regarding this Prior authorization, call
866-773-0695

Prior Authorization Vendor for ND

ND Medicaid requires that patients receiving a prescription for non-preferred medications to meet specific diagnosis and step-therapy requirements. Criteria for agents requiring prior authorization can be found at one of the following locations:

- The Preferred Drug List (PDL) available at www.hidesigns.com/assets/files/ndmedicaid/NDPDL.pdf
- Prior Authorization Criteria available at www.hidesigns.com/assets/files/ndmedicaid/2018/Criteria/PA_Criteria.pdf

*****Completed Medwatch form(s) must be attached to this request for failed trial(s) in which the active ingredient of the failed product is the same as the requested product*****

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name	Specialist involved in therapy (if not treating physician)		
Prescriber NPI	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage:	**Diagnosis for this request:**		
List all failed medications:		**Start Date:**	**End Date:**

Additional Qualifications for Coverage (e.g. medical justification explaining inability to meet required trials)

□ Patient is pregnant: Due Date _____
□ Patient has inability to take or tolerate solid oral dosage forms (please attach swallow study)
□ Patient has feeding tube in place: (please state specific type of feeding tube _____)
□ Other: (please fill out below)

□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*

Prescriber (or Staff) / Pharmacy Signature**	Date

**: *By completing this form, I hereby certify that the above request is true, accurate and complete. That the request is medically necessary, does not exceed the medical needs of the member, and is clinically supported in the patient's medical records. I also understand that any misrepresentations or concealment of any information requested in the prior authorization request may subject me to audit and recoupment.*

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Osteoporosis

Approval Duration:

Authorization will be for 2 years (1 year for Evenity)

Criteria:

- Patient must have an FDA approved indication for use
- Patient must have a current BMD T-score ≤ -2.5 OR new fracture after a 6-month trial of each of the following, as evidenced by paid claims or pharmacy print-outs:
    - Alendronate or Risedronate
    - Denosumab
- Patient must be at high risk of fracture, confirmed by at least one of the following:
    - BMD T-score ≤ -2.5 based on BMD measurements from lumbar spine, hip, or radius
    - History of low trauma fracture
    - Multiple risk factors for fracture

Additional Criteria for Forteo and Miacalcin:

- Patient must have a current BMD T-score ≤ -2.5 OR new fracture after a 6-month trial of each of the following, as evidenced by paid claims or pharmacy print-outs:
    - Evenity (Romosozumab)
    - Tymlos (Abaloparatide)

Preferred	Non-Preferred
Alendronate	EVENITY (Romosozumab)
Calcitonin, Salmon Nasal Spray	FORTEO (Teriparatide)
Ibandronate	MIACALCIN (Calcitonin, Salmon)
PROLIA (Denosumab)	TYMLOS (Abaloparatide)
Risedronate	

health information designs

Osteoporosis Agents
Prior Authorization Form

Fax Completed Form to:
855-207-0250
For questions regarding this Prior authorization, call
866-773-0695

Prior Authorization Vendor for ND

ND Medicaid requires that patients receiving a new prescription for non-preferred osteoporosis agents must meet the following criteria:

- Patient must have an FDA approved indication for use
  - Patient must have a current BMD T-score ≤ -2.5 OR new fracture after 6-month trials of each of the following:
    - Denosumab AND either Alendronate or Risedronate
- Patient must be at high risk of fracture, confirmed by at least one of the following:
  - BMD T-score ≤ -2.5 based on BMD measurements from lumbar spine, hip, or radius
  - History of low trauma fracture OR multiple risk factors for fracture
- Additional Criteria for Forteo and Miacalcin:
  - Patient must have a current BMD T-score ≤ -2.5 OR new fracture after 6-month trials of each of the following:
    - Evenity (Romosozumab) AND Tymlos (Abaloparatide)

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name	Specialist involved in therapy (if not treating physician)		
Prescriber NPI	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage:	**Diagnosis for this request:**		
List all failed medications:		**Start Date:**	**End Date:**

Qualifications for coverage:

Patient's BMD T-Score:	Site of BMD Measurement:

Does the patient have a history of low trauma fracture? □ YES □NO
Has the patient had a new fracture within the last 6-months? □ YES □NO
Does the patient have multiple risk factors for fracture? □ YES □NO

□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*

Prescriber (or Staff) / Pharmacy Signature**	Date

**: *By completing this form, I hereby certify that the above request is true, accurate and complete. That the request is medically necessary, does not exceed the medical needs of the member, and is clinically supported in the patient's medical records. I also understand that any misrepresentations or concealment of any information requested in the prior authorization request may subject me to audit and recoupment.*

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Hyperkalemia

Approval Duration:
Initial: 3 months
Renewal: 6 months

Initial Criteria:

- Patient must be 18 years of age or older.
- Medication must be prescribed by, or in consultation with, a cardiologist or nephrologist
- Patient's current serum potassium level must be exceeding the upper limit of normal, as evidenced by documentation from at least two separate lab values, submitted with the request
- Patient must not have gastrointestinal motility disorders (e.g. severe constipation, bowel obstruction or impaction, abnormal postoperative bowel motility disorders)
- One of the following criteria must be met:
    - Patient must have failed a 30-day trial with at least one preferred product
    - Provider has submitted evidenced-based, medical justification explaining why the patient is unable to use all available preferred agents.
- The patient must not be receiving the medications known to cause hyperkalemia listed below, OR medical justification must be provided explaining why discontinuation of these agents would be clinically inappropriate in this patient:
    - angiotensin-converting enzyme inhibitor
    - angiotensin II receptor blocker
    - aldosterone antagonist
    - nonsteroidal anti-inflammatory drugs (NSAIDs)

Renewal Criteria:

- Patient's current serum potassium level is within normal limits or has been significantly reduced from baseline, as evidenced by lab documentation submitted with the request

Preferred	Non-Preferred
Bumetanide	LOKELMA (Sodium Zirconium Cyclosilicate)
Chlorothiazide	VELTASSA (Patiromer)
Fludrocortisone	
Furosemide	
Hydrochlorothiazide	
Indapamide	
Metolazone	
Torsemide	

health information designs

Hyperkalemia
Prior Authorization Form

Fax Completed Form to:
855-207-0250
For questions regarding this Prior authorization, call
866-773-0695

Prior Authorization Vendor for ND

ND Medicaid requires that patients receiving a prescription for select agents for hhyperkalemia to meet the following criteria:

- Patient must be 18 years of age or older
- Medication must be prescribed by, or in consultation with, a cardiologist or nephrologist
- Patient's current serum potassium level must be exceeding the upper limit of normal (shown by 2 labs)
- Patient must not have gastrointestinal motility disorders
- One of the following criteria must be met:
  - Patient must have failed a 30-day trial with at least one preferred product
  - Provider has submitted medical justification explaining why the patient cannot use any preferred agents
- The patient must not be receiving the medications known to cause hyperkalemia, OR medical justification must be provided explaining why discontinuation of these agents would be clinically inappropriate in this patient
- **Renewal**: Patient's current serum potassium level must be within normal limits or significantly reduced from baseline

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name	Specialist involved in therapy (if not treating physician)		
Prescriber NPI	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage:	**Diagnosis for this request:**		
List all failed medications:		**Start Date:**	**End Date:**

Additional Qualifications for Coverage

Has the provider attached required lab documentation showing 2 of the patient's current potassium levels?	□ YES □NO
Does the patient have a diagnosis of any gastrointestinal motility disorder?	□ YES □NO
Is the patient to continue to receive a medication known to cause hyperkalemia?	□ YES □NO

□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*

Prescriber (or Staff) / Pharmacy Signature**	Date

**: *By completing this form, I hereby certify that the above request is true, accurate and complete. That the request is medically necessary, does not exceed the medical needs of the member, and is clinically supported in the patient's medical records. I also understand that any misrepresentations or concealment of any information requested in the prior authorization request may subject me to audit and recoupment.*

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Parkinson's disease

Initial Criteria:

- Patient must have an FDA approved indication for use
- Patient must be currently taking carbidopa – levodopa, as evidenced by paid claims or pharmacy print-outs, and will continue taking carbidopa – levodopa concurrently with requested agent

Additional Criteria for Gocovri, Osmolex ER, Rytary, and Pramipexole ER:

- Patient is not currently residing in a long-term care facility
- The prescriber must submit medical justification explaining why the patient cannot use the preferred product (subject to clinical review)

Additional Criteria for apomorphine, Duopa and Inbrija

- The provider must submit documentation of a swallow study or other medical documentation (e.g. chart notes) indicating that the patient has a proven inability to ingest solid dosage formulations.

Additional Criteria for Xadago

- Medication must be prescribed by, or in consultation with, a psychiatrist or neurologist
- Patient must be currently experiencing intermittent hypomobility or "off" episodes
- Patient must be exhibiting deterioration in quality of response, intermittent hypomobility, or "off" episodes during levodopa/carbidopa therapy
- Patient must have had inadequate response to rasagiline and selegiline, as evidenced by paid claims or pharmacy print-outs

Additional Criteria for Nuplazid

- Medication must be prescribed by, or in consultation with, a psychiatrist or neurologist
- Patient must be experiencing recurrent or continuous hallucinations and/or delusions for the past 30 days
- Patient must have experienced an inadequate response to a 30-day trial of quetiapine or clozapine, as evidenced by paid claims or pharmacy print-outs
- Patient must not have experienced a reduction in symptoms of psychosis, despite documented medication dosage reduction and discontinuation trials (with a goal of levodopa monotherapy)

Additional Criteria for Tolcapone

- Patient must have failed a 30-day trial of entacapone

health information designs

General
Prior Authorization Form

Fax Completed Form to:
855-207-0250
For questions regarding this Prior authorization, call
866-773-0695

Prior Authorization Vendor for ND

ND Medicaid requires that patients receiving a prescription for non-preferred medications to meet specific diagnosis and step-therapy requirements. Criteria for agents requiring prior authorization can be found at one of the following locations:

- The Preferred Drug List (PDL) available at www.hidesigns.com/assets/files/ndmedicaid/NDPDL.pdf
- Prior Authorization Criteria available at www.hidesigns.com/assets/files/ndmedicaid/2018/Criteria/PA_Criteria.pdf

*****Completed Medwatch form(s) must be attached to this request for failed trial(s) in which the active ingredient of the failed product is the same as the requested product*****

Part I: TO BE COMPLETED BY PHYSICIAN

Recipient Name	Recipient Date of Birth	Recipient Medicaid ID Number	
Prescriber Name	Specialist involved in therapy (if not treating physician)		
Prescriber NPI	Telephone Number	Fax Number	
Address	City	State	Zip Code
Requested Drug and Dosage:	**Diagnosis for this request:**		
List all failed medications:		**Start Date:**	**End Date:**

Additional Qualifications for Coverage (e.g. medical justification explaining inability to meet required trials)

□ Patient is pregnant: Due Date _____
□ Patient has inability to take or tolerate solid oral dosage forms (please attach swallow study)
□ Patient has feeding tube in place: (please state specific type of feeding tube _____)
□ Other: (please fill out below)

□ *I confirm that I have considered a generic or other alternative and that the requested drug is expected to result in the successful medical management of the recipient.*

Prescriber (or Staff) / Pharmacy Signature**	Date

**: *By completing this form, I hereby certify that the above request is true, accurate and complete. That the request is medically necessary, does not exceed the medical needs of the member, and is clinically supported in the patient's medical records. I also understand that any misrepresentations or concealment of any information requested in the prior authorization request may subject me to audit and recoupment.*

Part II: TO BE COMPLETED BY PHARMACY

PHARMACY NAME:			ND MEDICAID PROVIDER NUMBER:
TELEPHONE NUMBER	FAX NUMBER	DRUG	NDC #

Renewal Criteria:

- Patient has experienced disease stabilization or improvement in disease since initiation of treatment

Preferred	Non-Preferred
Amantadine	DUOPA (levodopa/carbidopa)
AZILECT (Rasagiline)	APOKYN (Apomorphine)
Benztropine	GOCOVRI (amantadine ER)
Bromocriptine	INBRIJA (Levodopa)
Carbidopa-levadopa-entacapone	Pramipexole ER
Carbidopa-Levadopa	NUPLAZID (pimavanserin)
Carbidopa-Levadopa ER	OSMOLEX ER (amantadine ER)
Entacapone	Rasagiline
Levodopa	RYTARY (levodopa/carbidopa)
NEUPRO (rotigotine) PATCH	Tolcapone
Pramipexole	XADAGO (Safinamide)
Ropinirole	
Ropinirole ER	
Selegiline	
Trihexyphenidyl	

REVIEW OF SHORT ACTING OPIOID ANALGESICS

SHORT-ACTING OPIOIDS:

- Opioid analgesic agents are the most commonly used pharmacologic agents for the treatment of moderate to severe pain
- **Mechanism**: Agonists at μ-opiate receptors in the CNS, causing inhibition of ascending pain pathways, altering the perception of and response to pain.
- Overall, evidence from comparative clinical trials suggests similar rates of efficacy between short acting agents when dosed at equipotent doses (see table of morphine equivalence)
- Unintentional drug overdose death rates in the United States have increased five-fold since 1990 and this has been driven by increased use of opioid analgesics
    - Pain management with short-acting opioids should be individualized for each patient and include an evaluation of patient patient specific factors that determine the best agent from a safety perspective.
- Short-acting opioid analgesic products are available in many dosage forms, varying potencies and differing durations of action
    - Available Oral Dosage Formulations for Pain (excluding IV)

	Tablet/Capsule	Solution	Suspension	Other
Benzhydrocodone/ APAP	X			
Codeine	X	X		
Codeine/APAP	X	X	X	
Fentanyl				**Fentora**: Buccal tablets: **Subsys**: SL spray **Lazanda**: Nasal spray **Actiq**: Transmucosal lozenge **Abstral**: SL tabs
Hydrocodone/ APAP	X	X		Elixer
Hydrocodone/ ibuprofen	X			
Hydromorphone	X	X		Suppository
Meperidine	X	X		
Morphine	X	X		Suppository
Oxycodone	X	X		
Oxycodone/ APAP	X	X		
Oxycodone/ ASA	X			
Oxycodone/ ibuprofen	X			
Oxymorphone	X			
Tapentadol	X			
Tramadol	X			
Tramadol/ APAP	X			

SAFETY PROFILE:

- **All Short-Acting Agents:**
    - HSR
    - Addiction, abuse, and misuse
    - Respiratory depression
        - Contraindicated in those with acute or severe bronchial asthma in an unmonitored setting
    - Risks from concomitant use with benzodiazepines or other CNS depressants
    - Neonatal withdrawal syndrome
    - Contraindicated in patients with GI obstruction due to constipation
    - CNS depression and sedation
    - Hypotension

- **Contraindicated in patients <12 years of age or <18 years for postoperative tonsillectomy and/or adenoidectomy management:**
    - Codeine
    - Tramadol

- **Use is contraindicated with concomitant monoamine oxidase inhibitor (MAOI) therapy or use within the last 14 days:**
    - Codeine
    - Meperidine
    - Morphine
    - Tapentadol
    - Tramadol

- **Recommended limited duration of use:**
    - Meperidine: avoid use for >48 hours
    - Benzhydrocodone: should not be used for >14 days

- **CYP 3A4 Interactions:**
    - Benzhydrocodone
    - Hydrocodone
    - Meperidine
    - Oxycodone
    - Tramadol
    - Hydromorphone, morphine, oxymorphone, oxycodone, and fentanyl are potent schedule II controlled opioid agonists that have the highest potential for abuse and risk of producing respiratory depression.

- **Other Safety Concerns:**
    - **Meperidine, Tramadol & Tapentadol**
        - Serotonin syndrome (due to SNRI effects)
    - **Oxycodone:**
        - Contraindicated in patients with moderate to severe hepatic impairment
    - **Oxymorphone:**
        - Contraindicated in hypercarbia
    - **Meperidine:**
        - Use with caution in patients with atrial flutter and other supraventricular tachycardias
        - Generates an active metabolite (normeperidine) which can accumulate and precipitate anxiety, tremors, or seizures
            - Risk increases with preexisting CNS or renal dysfunction, prolonged use (more than 48 hours), and cumulative dose (>600 mg/24 hours in adults)
            - **PER LABEL:** Oral meperidine should not be used since first-pass metabolism decreases efficacy while increasing normeperidine concentrations
                - Naloxone does not reverse, and may even worsen, neurotoxicity.

MME CONVERSION FACTORS

Drug name (strength units) MME Conversion Factor	Type of Opioid (strength units) MME Conversion Factor
Benzhydrocodone (mg)	1.2
Codeine (mg)	0.15
Hydrocodone (mg)	1
Hydromorphone (mg)	4
Levorphanol tartrate (mg)	11
Meperidine hydrochloride (mg)	0.1
Morphine	1
Oxycodone (mg)	1.5
Oxymorphone (mg)	3
Tapentadol (mg)	0.4
Tramadol (mg)	0.1

CURRENT UTILIZATION

ND Medicaid Utilization (06/2018 – 05/2019)		
Label Name	**Rx Num**	**Total Reimb Amt**
Benzhydrocodone/ APAP	-	-
Codeine	-	-
Codeine/APAP	662	$11,353.32
Fentora	-	-
Actiq	-	-
Subsya	-	-
Lazanda	-	-
Abstral	-	-
Hydrocodone/ APAP	6,559	$164,206.16
Hydrocodone/ ibuprofen	71	$1,758.44
Hydromorphone	234	$42,78.17
Meperidine	9	$155.81
Morphine	185	$5,207.16
Oxycodone	1,837	$34,412.04
Oxycodone/ APAP	2,972	$81,575.14

Oxymorphone	-	-
Tapentadol	5	$2,042.33
Tramadol	2,452	$37,990.69
Tramadol/ APAP	78	$1,141.7

REFERENCES:

1. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on May 2. 2019.
2. Apadaz (benzhydrocodone/acetaminophen) [prescribing information]. Newton, PA: KVK-Tech Inc; January 2019.
3. National Center for Injury Prevention and Control. CDC compilation of benzodiazepines, muscle relaxants, stimulants, zolpidem, and opioid analgesics with oral morphine milligram equivalent conversion factors, 2016 version. Atlanta, GA: Centers for Disease Control and Prevention; 2016. Available at https://www.cdc.gov/drugoverdose/media/. For more information Lokelma (sodium zirconium cyclosilicate) [prescribing information]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; July 2018.

REVIEW OF AGENTS FOR TREATMENT OF THROMBOCYTOPENIA

THROMBOCYTOPENIA:

- Thrombocytopenia is defined as a platelet count below the lower limit of normal (<150,000/µL).
  - Mild: PLT of 100,000 to 150,000/µL
  - Moderate: PLT of 50,000 to 99,000/µL
  - Severe: PLT of <50,000/µL)
- Associated low platelet counts carry risks that may range from life-threatening bleeding to no risk at all, depending on comorbid conditions and the cause of thrombocytopenia.
  - Clinical predictors of bleeding include prior bleeding at a similar platelet count and the presence of wet purpura (eg, in mucosal membranes).
    - Surgical bleeding generally may be a concern with platelet counts <50,000/µL (<100,000/µL for some high-risk procedures such as neurosurgery or major cardiac or orthopedic surgery).
    - Severe spontaneous bleeding is most likely with platelet counts <20,000 to 30,000/µL, especially below 10,000/µL.
- Often caused by one of a variety of conditions, with associated risks that range from life-threatening to none.
  - Typically caused by:
    - **Decreased platelet production in the bone marrow:**
      - Bone marrow disorders that impair platelet production (eg, nutrient deficiencies, myelodysplastic syndromes, infection/sepsis)
    - **Peripheral platelet destruction by antibodies:**
      - Anti-platelet antibodies occur in primary immune thrombocytopenia ITP and also in secondary ITP (e.g. from another autoimmune syndrome such as SLE).
    - **Platelet consumption in thrombi:**
      - Occurs in disseminated intravascular coagulation (DIC), thrombocytopenic purpura (TTP), & hemolytic uremic syndrome (HUS).
    - **Dilution:**
      - Typically caused by fluid resuscitation or massive transfusion.
    - **Sequestration (pooling) of platelets in the spleen:**
      - Conditions that increase spleen size or cause splenic congestion through portal hypertension (eg, cirrhosis, alcoholic liver disease) can decrease the platelet count without altering the total platelet mass in the body.
- **Immune thrombocytopenia (ITP):**
  - Common cause of moderate to severe thrombocytopenia in an otherwise asymptomatic adult.
  - Other cell lines are unaffected (ie, ITP does not cause anemia or leukopenia).
  - The prevailing understanding of the mechanism of ITP is antibody-mediated platelet destruction. However, anti-platelet antibodies are not always detected, and their testing is not clinically useful.
  - A presumptive diagnosis of ITP is made when the history, physical examination, and laboratory data do not suggest an alternative diagnosis.

DRUG TREATMENTS:

- **Chronic immune thrombocytopenia (ITP)**
  - **FIRST-LINE AGENTS:**
    - **Glucocorticoids** raise the platelet count in approximately 2/3 of patients, with complete long-term remissions with glucocorticoids have been reported in approximately 20%.
      - Long-term glucocorticoid administration should be avoided, as the consequences may be severe and several alternatives are available.
    - **IVIG** can raise the platelet count within 24 to 48 hours in most patients with ITP, which will usually persist for 2-6 weeks
    - **Anti-D** (anti-D, WinRho, RhoGAM, Rho(D) immune globulin) is an alternative to conventional IVIG for patients whose red blood cells (RBCs) are Rh(D) positive.

- **2ND LINE:**
  - **THROMBOPOIETIN RECEPTOR AGONISTS (TPO-RAs)**
    - Small-molecule peptide and non-peptide agents that bind to and activate TPO receptor, stimulating the production of platelets in the bone marrow.
    - Generally, platelet counts increase in approximately 7 to 14 days.
    - Once treatment is D/C, PLT generally return to baseline levels or even below baseline.

- **Promacta (eltrombopag):**
  - Treatment of thrombocytopenia in adult & pediatric patients ≥1 year of age with who have had an insufficient response to corticosteroids, immunoglobulins, or splenectomy.
    - Should only be used if the degree of thrombocytopenia & clinical condition increase the risk for bleeding.
    - Use the lowest dose necessary to achieve & maintain platelet count ≥50,000/mm3.
    - D/C if platelet count does not respond to a level to avoid clinically important bleeding after 4 weeks at the maximum recommended dose.

- **Nplate (romiplostim):**
  - Treatment of adult patients with chronic ITP (pediatric patients with ITP for ≥6 months) who have had insufficient response to corticosteroids, immunoglobulins, or splenectomy.
    - D/C if platelet count does not increase to a level sufficient to avoid clinically important bleeding after 4 weeks at the maximum recommended dose of 10 mcg/kg/week.
    - Should only be used when the degree of thrombocytopenia & clinical condition increase the bleeding risk; should not be used in attempt to normalize platelet counts.
    - REMS Program: Risks of progression of myelodysplastic syndromes to AML, thrombotic/thromboembolic complications, bone marrow fibrosis/reticulin formation, worsened thrombocytopenia after cessation of romiplostim therapy, & medication errors associated with serious outcomes.

  - **SPLEEN TYROSINE KINASE (Syk) INHIBITOR:**
    - Inhibits the signal transduction of Syk, which affects cellular proliferation, differentiation, survival and immune regulation via IgG and B-cell receptor signaling and autoantibody production. Through this action, Syk inhibitors reduce antibody-mediated destruction of platelets.
    - **Tavalisse (fostamatinib):**
      - Treatment of thrombocytopenia in adults with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.
        - D/C after 12 weeks if platelet count does not increase to a level sufficient to avoid clinically important bleeding.
        - Dose adjustments on to achieve & maintain platelet count of at least 50,000/mm3 & based on experienced ADRs.
        - If ADRs would cause dose reduction below 100 mg/day is required, D/C.

- **<u>Chronic liver disease-associated thrombocytopenia</u>**
  - Treatment primarily consists of non-pharmacologic therapies (weight loss, control of DM, etc), with pharmacologic treatments limited to those areas.
  - **TPO-RAs:** Used only when a patient is scheduled to undergo a procedure that puts the patient at risk of bleeding:
    - **Doptelet (avatrombopag):**
      - Do not use to normalize platelet counts.
      - Begin 10 to 13 days prior to the procedure.
      - Obtain a platelet count prior to therapy & on the day of the procedure.
    - **Mulpleta (lusutrombopag):**
      - Do not use to normalize platelet counts in patients with chronic liver disease.
      - Begin 8 to 14 days prior to the procedure.
      - Obtain a platelet count prior to therapy & within 2 days of the procedure.

- **Chronic hepatitis C infection-associated thrombocytopenia**
  - **Promacta (eltrombopag):**
    - Treatment of thrombocytopenia in patients with chronic hepatitis C to allow the initiation & maintenance of interferon-based therapy.
      - Should only be used if the degree of thrombocytopenia prevents initiation of or limits the ability to maintain interferon-based therapy (d/c if antiviral therapy is D/Cd).

Summary of Available TPO-RAs and Syk Inhibitors					
	Promacta	**Doptelet**	**Mulpleta**	**Nplate**	**Tavalisse**
Chronic ITP	X			X	X (refractory)
Chronic liver disease-associated thrombocytopenia		X	X		
Chronic HCV-associated thrombocytopenia	X				
Administration	Oral w/o food	Oral w/ food	Oral w/ or w/o food	SubQ	Oral w/ or w/o food
Normal Dosing	≥18: 25/100 mg 1-17: 12.5-75 mg	40-60 mg	3 mg	1-10 mcg/kg	100-150 mg
Frequency	Daily	Daily for 5 days	Daily for 7 days	Weekly	Twice daily
Adjustments	Based on PLT, genetics, & hepatic function	Based on PLT	None	Based on PLT	Based on PLT & ADRs
Ages	≥1 years	≥18 years	≥18 years	≥1 years	≥18 years
Additional concerns	▪ Hepatotoxicity ▪ Thromboembolism ▪ Cataract	▪ Thromboembolism	▪ Thromboembolism	▪ Malignancy ▪ Thromboembolism ▪ Bone marrow reticulin fiber form.	▪ Hypertension ▪ GI Toxicity ▪ Neutropenia ▪ Hepatotoxicity

COST

Drug	Strength	Package Size	AWP Pkg Price	AWP Unit Price
Doptelet	20 mg tab	10	$11,328.00	$1,132.80
Mulpleta	3 mg tab	7	$10,200.00	$1,457.15
Promacta	12.5 mg powder	30 packets	$5,911.76	$197.06
Promacta	12.5 mg tab	30	$5,911.76	$197.06
Promacta	25 mg tab	30	$5,911.76	$197.06
Promacta	50 mg tab	30	$10,698.41	$356.61
Promacta	75 mg tab	30	$16,047.61	$534.92
Tavalisse	100 mg tab	60	$11,793.60	$196.56
Tavalisse	150 mg tab	60	$11,793.60	$196.56
Nplate	250 mcg injection	1	$2,230.30	$2,230.30
Nplate	500 mcg injection	1	$4,460.59	$4,460.59

CURRENT UTILIZATION

ND Medicaid Utilization (06/2018 – 05/2019)		
Label Name	**Rx Num**	**Total Reimb Amt**
Doptelet	-	-
Mulpleta	-	-
Promacta	5	$31,345.59
Tavalisse	-	-
Nplate	-	-

REFERENCES:

1. Facts & Comparisons eAnswers. Available at http://online.factsandcomparisons.com. Accessed on May 2. 2019.
2. Nplate (romiplostim) [prescribing information]. Thousand Oaks, CA: Amgen; December 2018.
3. Tavalisse (fostamatinib) [prescribing information]. South San Francisco, CA: Rigel Pharmaceuticals, Inc; April 2018.
4. Promacta (eltrombopag) [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals; April 2019.
5. Mulpleta (lusutrombopag) [prescribing information]. Florham Park, NJ: Shionogi Inc; July 2018.
6. Doptelet (avatrombopag) [prescribing information]. Durham, NC: AkaRx, Inc; March 2019.
7. UpToDate. Available at https://www.uptodate.com. Accessed on May 20, 2019.

REVIEW OF AGENTS FOR TREATMENT OF INTERSTITIAL CYSTITIS

INTERSTITIAL CYSTITIS:

- Interstitial cystitis/bladder pain syndrome (IC/BPS) is a condition involving chronic bladder pain or discomfort that can have a profound detrimental impact on quality of life
- Diagnosis of IC/BPS applies to patients with chronic bladder pain in the absence of other etiologies of the symptoms, and the American Urological Association definition of IC/BPS requires that the duration of symptoms is at least 6 weeks
- Symptoms:
    - Persistent unpleasant sensations (described as pain, pressure, or discomfort) that are attributable to the bladder that can vary
        - Most consistent feature is an increase in discomfort with bladder filling and a relief with voiding. This can vary from mild pressure to severe, debilitating pain.
        - Other symptoms:
            - Urinary urgency
            - Increased frequency of urination
            - Suprapubic, urethral, and/or perineal pain
            - Dysuria
            - Sensation of bladder spasms/pressure
            - Gross hematuria
    - Majority of patients' symptoms that are of gradual onset, with worsening of discomfort, urgency and frequency over a period of months
- The pathophysiology of IC/BPS bladder pain is not well understood, and it is likely that such symptoms represent more than one underlying etiology

TREATMENT FOR INTERSTITIAL CYSTITIS:

- Treatment goal of providing symptomatic relief

First-line: Self-care and behavior modification

- Application of local heat or cold over the bladder or perineum.
- Avoidance of activities or food or beverages that exacerbate symptoms
- Fluid management (restriction or increased fluid intake)
- Bladder training with urge suppression
- Non-absorbed, cation exchange polymer that increases fecal potassium excretion through binding of potassium in the lumen of the GI tract.

Second-Line: Oral medications

- There are no large comparative studies of oral medications for IC/BPS.
- **Amitriptyline:**
    - **Effects**: Believed to have analgesic properties and relieves the depressive symptoms associated with chronic pain
    - **Use**: Most widely used agent for initial pharmacologic therapy of IC/BPS, as the effects can be observed soon after therapy.
    - **Data**: A randomized trial (n = 50) found that 4 months of amitriptyline (25-100 mg daily) resulted in a significantly higher proportion of patients than placebo with a >30% decrease in a symptom score (42% vs. 13%). Another randomized trial (n = 271) of 12 weeks of amitriptyline therapy (10-75 mg once daily) failed to demonstrate significant increase in the rate of moderate or marked symptom improvement against placebo (55% vs. 45%), however, a significantly higher rate of improvement was observed in the subgroup of patients (n = 106) who were able to tolerate doses of ≥50 mg daily (77% vs. 53%).
    - **Dosing**: Amitriptyline appears to be most effective at higher doses but use of these doses is limited by bothersome or dangerous adverse effects.
        - Typical dosing regimen: starts at 10 mg qhs, escalating at weekly intervals to 25, 50, and 75 mg (or to the maximum tolerated dose).
    - **ADRs**: Adverse effects include anticholinergic effects (eg, dry mouth, urinary retention); sedation; weight gain; orthostatic hypotension; and cardiac conduction abnormalities.

- **Warnings/Precautions:** Do not use with MAOIs or cisapride. Avoid use with CYP 450 inhibitors.

- **Elmiron (pentosan polysulfate sodium):**
  - **Effects**: the drug appears to adhere to the bladder wall mucosa where it may act as a buffer to protect the tissues from irritating substances in the urine
  - **Use**: Only agent that is specifically FDA-approved for treatment of IC/BPS. The typical regimen is 100 mg three times daily. May take 3-6 months after initiation to experience symptom relief.
  - **Data**: A meta-analysis of five randomized trials found that PPS resulted in a significantly higher rate of clinical improvement than placebo, although the magnitude of effect was modest (relative risk [RR] 1.69, 95% CI 1.16-2.46).
  - **Dosing:** Recommended dosing is 100 mg three times daily.
  - **ADRs**: May be associated with hair loss, although this side effect is mild and reversible. Rarely, it has been associated with mild elevation in liver function enzymes, and it is recommended to obtain these blood tests after six months of therapy. In our practice, we do not continue monitoring liver function enzymes if the initial testing at six months is normal.
  - **Warnings/Precautions:** Bleeding complications of ecchymosis, epistaxis, and gum hemorrhage have been reported (mild anticoagulant); May cause immunoallergic thrombocytopenia; Alopecia is associated with Elmiron; Do not use in patients with known history of HSR to heparin agents.
- **Antihistamines:**
  - Hydroxyzine is the most commonly used antihistamine for the treatment of IC/BPS
  - **Use:** Most commonly used in patients who patients who also have an allergic disorder, and it those who complain of insomnia because they void frequently during the night.
  - **Effects:** reduces histaminergic reactions, and potential benefit is hypothesis that hypersensitivity is a part of the pathogenesis of IC/BPS.
  - **Data:** The only randomized trial (31 patient assigned to hydroxyzine, 31 to placebo) to evaluate this therapy did not find a significantly higher response rate with hydroxyzine compared with placebo (31% versus 20%).
  - **Dosing:** 25 to 50 mg at bedtime.
  - **ADRs:** Most common include sedation, dizziness, and drowsiness.
  - **Warnings/Precautions:** QT prolongation; Acute generalized exanthematous pustulosis; May worsen glaucoma; May cause respiratory depression.

COST

Drug	Strength	Package Size	AWP Pkg Price	AWP Unit Price
Amitriptyline	10 mg tab	100	$31.80	$0.32
Amitriptyline	25 mg tab	100	$63.60	$0.64
Amitriptyline	50 mg tab	100	$127.00	$1.27
Amitriptyline	75 mg tab	100	$190.80	$1.91
Amitriptyline	100 mg tab	100	$254.00	$2.54
Amitriptyline	150 mg tab	100	$381.00	$3.81
Elmiron	100 mg caps	100	$1,105.42	$11.05
Hydroxyzine	10 mg tab	100	$63.50	$0.64
Hydroxyzine	25 mg tab	100	$91.98	$0.92
Hydroxyzine	50 mg tab	100	$111.55	$1.12

CURRENT UTILIZATION

ND Medicaid Utilization (06/2018 – 05/2019)		
Label Name	**Rx Num**	**Total Reimb Amt**
Amitriptyline	2,017	$64,759.06
Elmiron	51	$30,364.73
Hydroxyzine	2,450	$77,930.36

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3. Hanno PM, Erickson D, Moldwin R, et al. Diagnosis and treatment of interstitial cystitis/bladder pain syndrome: AUA guideline amendment. J Urol 2015; 193:1545.
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6. Forsell T, Ruutu M, Isoniemi H, et al. Cyclosporine in severe interstitial cystitis. J Urol 1996; 155:1591.
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REVIEW OF AGENTS FOR TREATMENT OF NARCOLEPSY

NARCOLEPSY:

- Narcolepsy is a chronic sleep disorder characterized by overwhelming daytime drowsiness and sudden attacks of sleep. People with narcolepsy often find it difficult to stay awake for long periods of time, regardless of the circumstances, and can occur with a sudden loss of muscle tone (type 1 narcolepsy) or without this cataplexy (type 2 narcolepsy)
- Narcolepsy is a chronic condition for which there's no cure. However, medications and lifestyle changes can help you manage the symptoms.
- **Symptoms**
  - Excessive daytime sleepiness/sudden falling asleep
  - Decreased alertness and focus throughout the day
  - In type 1 narcolepsy: sudden loss of muscle tone (cataplexy) including slurred speech to complete weakness of most muscles, and may last up to a few minutes
    - Triggered by intense emotions (e.g. laughter, excitement, fear, surprise or anger)
  - Sleep paralysis: a temporary inability to move or speak while falling asleep or upon waking
  - Rapid transition to REM sleep, usually within 15 minutes of falling asleep
  - Hallucinations when falling asleep or waking
- **Causes**
  - The exact cause of narcolepsy is unknown. Potentially due to low levels of hypocretin, which helps regulate wakefulness and REM sleep
- **Normal sleep pattern vs. narcolepsy**
  - Normal sleep: process begins with non-rapid eye movement (NREM) sleep, in which brain waves slow considerably. This transitions to REM sleep after ~1 hour
  - Narcolepsy: suddenly entering into REM sleep without first experiencing NREM sleep, both at night and during the day

DRUG TREATMENT FOR NARCOLEPSY:

- Goals: To obtain "normal" alertness during conventional waking hours or to maximize alertness at important times of the day (eg, during work, school, or while driving)

- **Currently Available, FDA-Approved Agents:**

	modafinil (Provigil) / armodafinil (Nuvigil)	**Methylphenidate**	**Amphetamines**	**sodium oxybate (Xyrem)**
MoA	Blocks reuptake of DA into presynaptic neurons	Blocks reuptake of DA & NE into presynaptic neurons	Blocks reuptake of DA & NE into presynaptic neurons	Metabolite of GABA; inhibitory effects on GABA-B receptors
Effects	Promotes wakefulness into early evening	Promotes wakefulness	Most potent wakefulness-promoting drugs	Reduces cataplexy and may decrease daytime sleepiness
Dosing	Dosed once daily	Dosed once or multiple times daily depending on product used	Dosed once or multiple times daily depending on product used	6-9 g in 2 divided doses at night: 1st qhs; 2nd 2.5-4 hours later
CIs	HSR	HSR; use during or within 14 days following MAOI; marked anxiety, tension, and agitation; glaucoma; Tourette syndrome or tics	HSR; use during or within 14 days following MAOI; marked anxiety, tension, and agitation; glaucoma; Tourette syndrome or tics	Coadministration with alcohol or sedative hypnotic agents; succinic semialdehyde dehydrogenase deficiency
Warning	SJS; potential for abuse	Potential for abuse and dependence.	High potential for abuse and dependence.	↑ anxiety, confusion, psychosis, agitation, depression, sleepwalking; Abuse potential
Caution	Psychosis, depression, or mania; CV disease; Tourette syndrome	CV disease; pre-existing psychosis; Seizure; PVD	CV disease; pre-existing psychosis; Seizure; PVD	Compromised respiratory function; CV Disease
ADRs	HA, nausea, dry mouth, anorexia, and diarrhea	↑ BP, palpitations, HA, insomnia, nervousness, restlessness, anxiety, anorexia	↑ BP, palpitations, HA, insomnia, nervousness, restlessness, anxiety, anorexia	Confusion, HA, Dizziness, N/V, weight loss, urinary incontinence, worsening of depression, sleepwalking

Newly FDA-Approved Agent:

- **Sunosi (solriamfetol):** FDA approved in March 2019, expected to be on the market in 2019.
  - **MoA:** selective dopamine and norepinephrine reuptake inhibitor with wake-promoting effects
  - **Indication:** To improve wakefulness in adult patients with excessive daytime sleepiness associated with narcolepsy or obstructive sleep apnea (OSA).
  - **Dosing:**
    - Initial dose: 75 mg once daily in the morning
      - May be increased to a max dose of 150 mg daily after 3 days (as tolerated)
  - **CI:** Concomitant use with/within 14 days of an MAOI
  - **Warnings/Precautions:**
    - May cause dose-dependent increases in blood pressure and heart rate
    - Psychiatric symptoms including anxiety, insomnia, and irritability have been reported with use
  - **ADRs:** Most common are headache, nausea, and decreased appetite

COST

Drug	Strength	Package Size	AWP Pkg Price	AWP Unit Price
armodafinil	250 mg tab	60	$1,967.73	$21.86
modafinil	200 mg tab	100	$3,994.48	$39.90
Concerta ER	54 mg tabs	100	$1,599.83	$15.99
Vyvanse	70 mg caps	100	$1,215.36	$12.15
Xyrem	500 mg/mL sln	180 mL	$5,540.93	$30.78
Sunosi	N/A	N/A	N/A	N/A

CURRENT UTILIZATION

ND Medicaid Utilization (06/2018 – 05/2019)		
Label Name	**Rx Num**	**Total Reimb Amt**
armodafinil	45	$1,607.72
modafinil	80	$2,605.81
Methylphenidate	12,610	$1,865,026.96
Vyvanse	6,398	$1,451,091.17
Amphetamine/ dextroamphetamine	5,965	$478,601.14
Xyrem	2	$24,875.40
Sunosi	-	-

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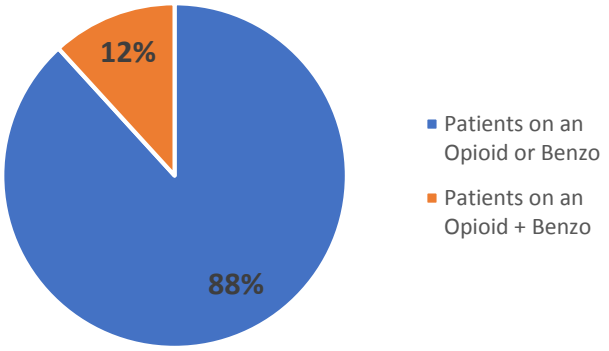
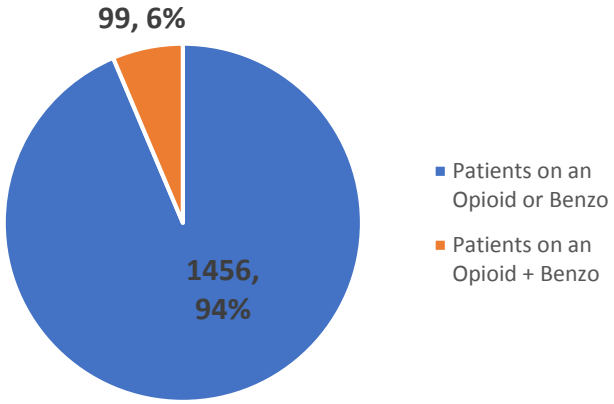
3. Adderall XR (dextroamphetamine/amphetamine) [prescribing information]. Lexington, MA: Shire US Inc; July 2018.
4. Ritalin/Ritalin SR [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals; January 2019.
5. Xyrem (sodium oxybate) [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals; October 2018.
6. Nuvigil (armodafinil) [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc; November 2018.
7. Sunosi (solriamfetol) [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals Inc; March 2019.

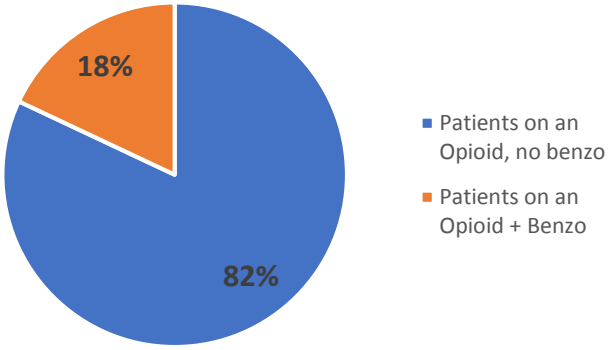
2018: % of Patients on Opioid or Benzo



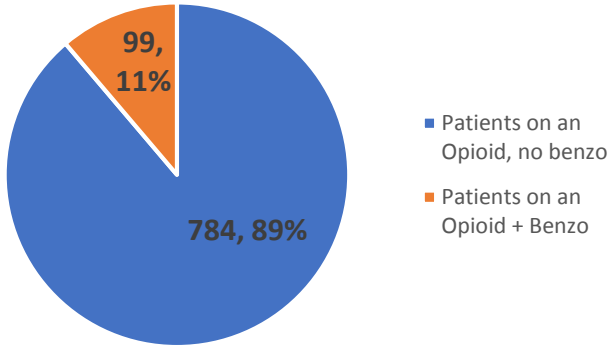
% of Patients on Opioid or Benzo



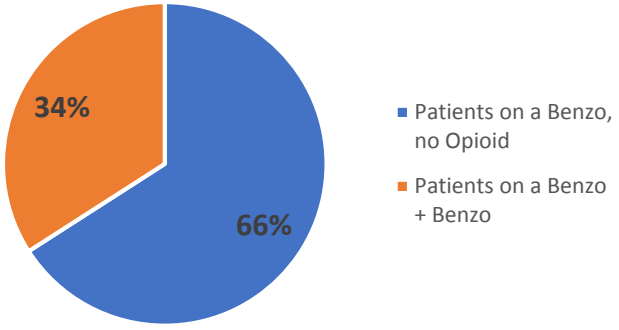
2018: % of Patients on Opioid also on Benzo



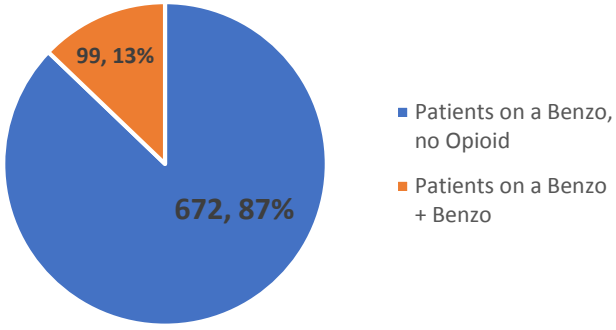
2019: % of Patients on Opioid also on Benzo

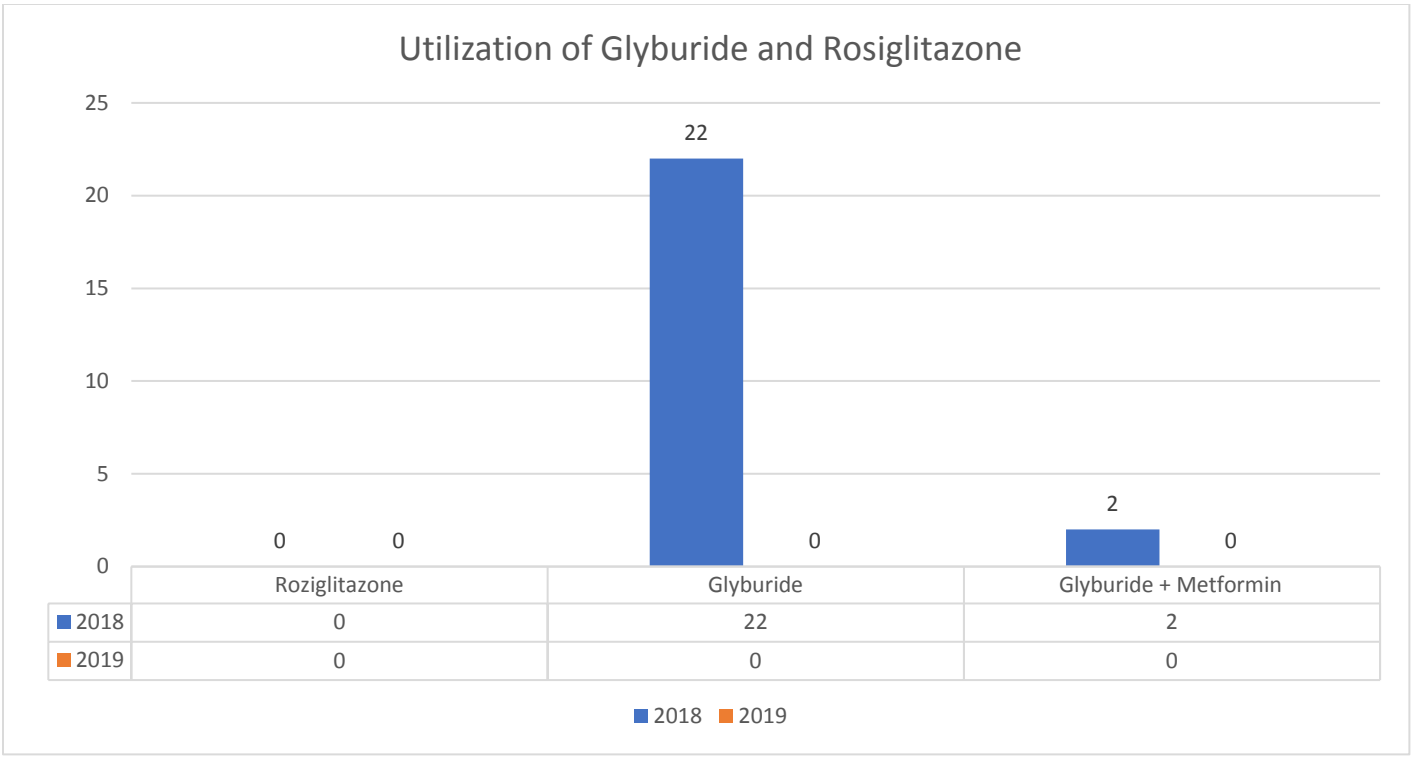


2018: % of Patients on Benzo also on Opioid



2019: % of Patients on Benzo also on Opioid




Utilization of Glyburide and Rosiglitazone
25
20
15
10
5
0
22
2
0
0
0
0
Roziglitazone
Glyburide
Glyburide + Metformin
2018
0
22
2
2019
0
0
0
2018
2019

NORTH DAKOTA MEDICAID
RETROSPECTIVE DRUG UTILIZATION REVIEW
CRITERIA RECOMMENDATIONS
2ND QUARTER 2019

Criteria Recommendations ***Approved*** ***Rejected***

1. Talazoparib / Overutilization _____ _____
Alert Message: The recommended dose of Talzenna (talazoparib) is 1 mg orally once daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Talazoparib		CKD Stage 3

Max Dose: 1 mg/day

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Talzenna Prescribing Information, October 2018, Pfizer, Inc.

2. Talazoparib / Therapeutic Appropriateness _____ _____
Alert Message: Talzenna (talazoparib) may be over-utilized. For patients with moderate renal impairment (CLcr 30 - 59 mL/min), the recommended dose of talazoparib is 0.75 mg once daily. Talazoparib has not been studied in patients with severe renal impairment (CLcr < 30 mL/min) or patients requiring hemodialysis.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Talazoparib 1mg		CKD Stage 3

Max Dose: 0.75mg/day

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Talzenna Prescribing Information, October 2018, Pfizer, Inc.

3. Talazoparib / Pregnancy / Pregnancy Negating _____ _____
Alert Message: Based on its mechanism of action and findings from animal data, Talzenna (talazoparib) can cause fetal harm when administered to a pregnant woman. Apprise pregnant women and females of reproductive potential of the potential risk to a fetus.

Conflict Code: MC – Drug (Actual) Disease Precaution
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Talazoparib	Pregnancy	Miscarriage
		Delivery
		Abortion

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Talzenna Prescribing Information, October 2018, Pfizer, Inc.

4. Talazoparib / Therapeutic Appropriateness _____ _____

Alert Message: Advise females of reproductive potential to use effective contraception during treatment and for at least 7 months following the last dose of Talzenna (talazoparib). Based on its mechanism of action and findings from animal data, talazoparib can cause fetal harm when administered to a pregnant woman.

Conflict Code: MC – Drug (Actual) Disease Precaution
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Talazoparib		Contraceptives

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Talzenna Prescribing Information, October 2018, Pfizer, Inc.

5. Talazoparib / Lactation _____ _____

Alert Message: There are no data on the presence of Talzenna (talazoparib) in human milk, the effects of the drug on milk production, or the effects of the drug on the breastfed child. Because of the potential for serious adverse reactions in a breastfed child from talazoparib, advise lactating women not to breastfeed during treatment with talazoparib and for at least 1 month after the final dose.

Conflict Code: MC – Drug (Actual) Disease Precaution
Drugs/Diseases

Util A	Util B	Util C
Talazoparib	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Talzenna Prescribing Information, October 2018, Pfizer, Inc.

6. Talazoparib / Males _____ _____

Alert Message: Based on genotoxicity and animal reproduction studies, advise male patients with female partners of reproductive potential and pregnant partners to use effective contraception during treatment with Talzenna (talazoparib) and for at least 4 months following the last dose.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Talazoparib		

Gender: Male

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Talzenna Prescribing Information, October 2018, Pfizer, Inc.

7. Talazoparib / Certain P-gp Inhibitors _____ _____

Alert Message: Coadministration with certain P-gp inhibitors (i.e., amiodarone, carvedilol, clarithromycin, itraconazole, or verapamil) may significantly increase Talzenna (talazoparib) exposure. If coadministration of talazoparib with one of these P-gp inhibitors cannot be avoided, reduce the talazoparib dose to 0.75 mg once daily. When the P-gp inhibitor is discontinued, increase the talazoparib dose (after 3 - 5 half-lives of the inhibitor) to the dose used prior to the initiation of the P-gp inhibitor.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Talazoparib 1 mg	Amiodarone	
	Carvedilol	
	Clarithromycin	
	Itraconazole	
	Verapamil	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Talzenna Prescribing Information, October 2018, Pfizer, Inc.

8. Talazoparib / Other P-gp Inhibitors _____ _____

Alert Message: Coadministration of Talzenna (talazoparib), a P-gp substrate, with the identified P-gp inhibitor may result in increased talazoparib exposure. Monitor the patient for talazoparib-related adverse reactions.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Talazoparib	Dronedarone	Cobicistat	
	Lapatinib	Ritonavir	
	Propafenone	Saquinavir	
	Quinidine	Ranolazine	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Talzenna Prescribing Information, October 2018, Pfizer, Inc.

9. Talazoparib / BCRP Inhibitors _____ _____

Alert Message: Coadministration of Talzenna (talazoparib), a BCRP substrate, with a BCRP inhibitor may result in increased talazoparib exposure. If coadministration cannot be avoided, monitor the patient for talazoparib-related adverse reactions.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B			Util C
Talazoparib	Cyclosporine	Elbasvir/Grazoprevir	Rolapitant	Teriflunomide
	Nelfinavir	Eltrombopag	Safinamide	Vemurafenib
	Atazanavir	Fostamatinib	Sirolimus	Velpatasvir/Sofosbuvir
	Daclatasvir	Glecaprevir/Pibrentasvir	Sulfasalazine	
	Leflunomide	Ledipasvir/Sofosbuvir	Tacrolimus	
	Osimertinib	Regorafenib	Tedizolid	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Talzenna Prescribing Information, October 2018, Pfizer, Inc.

10. Talazoparib / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Talzenna (talazoparib) have not been established in pediatric patients.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Talazoparib		

Age Range: 0-17 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Talzenna Prescribing Information, October 2018, Pfizer, Inc.

11. Apalutamide / Overutilization _____ _____

Alert Message: Erleada (apalutamide) may be over-utilized. The recommended dosage of apalutamide is 240 mg (four 60 mg tablets) orally once daily.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Apalutamide		

Max Dose: 240 mg/day

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Erleada Prescribing Information, Feb. 2018, Janssen Products.

12. Apalutamide / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Erleada (apalutamide) is contraindicated for use in pregnant women because the drug can cause fetal harm and potential loss of pregnancy. Apalutamide is not indicated for use in females, so animal embryo-fetal developmental toxicology studies were not conducted with apalutamide. Based on its mechanism of action, apalutamide may cause fetal harm when administered during pregnancy.

Conflict Code: MC – Drug (Actual) Disease Precaution/Warning
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Apalutamide	Pregnancy	Miscarriage
		Delivery
		Abortion

Gender: Female
Age Range: 11 – 50

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Erleada Prescribing Information, Feb. 2018, Janssen Products.

13. Apalutamide / Falls & Fractures _____ _____

Alert Message: Falls and fractures occurred in patients receiving Erleada (apalutamide). Evaluate patients for fracture and fall risk. Monitor and manage patients at risk for fractures according to established treatment guidelines and consider use of bone-targeted agents. In clinical trials, fractures occurred in 12% of patients treated with apalutamide and in 7% of patients treated with placebo.

Conflict Code: MC – Drug (Actual) Disease Precaution/Warning
Drugs/Diseases

Util A	Util B	Util C
Apalutamide	Falls	
	Fractures	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Erleada Prescribing Information, Feb. 2018, Janssen Products.

14. Apalutamide / Seizures _____ _____

Alert Message: Seizures have been reported in patients receiving Erleada (apalutamide). Permanently discontinue apalutamide in patients who develop a seizure during treatment. It is unknown whether anti-epileptic medications will prevent seizures with apalutamide. Advise patients of the risk of seizures while receiving apalutamide and of engaging in any activity where sudden loss of consciousness could cause harm to themselves or others.

Conflict Code: MC – Drug (Actual) Disease Precaution/Warning
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Apalutamide		Seizures
		Epilepsy

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Erleada Prescribing Information, Feb. 2018, Janssen Products.

15. Apalutamide / Strong CYP2C8 and CYP3A4 Inhibitors _____ _____

Alert Message: Co-administration of Erleada (apalutamide) with a strong CYP2C8 or CYP3A4 inhibitor is predicted to increase the steady-state exposure of the active moieties (sum of unbound apalutamide plus the potency-adjusted unbound N-desmethyl-apalutamide) of apalutamide. No initial dose adjustment is necessary; however, reduce the apalutamide dose based on tolerability.

Conflict Code: DD – Drug/ Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Apalutamide	Clarithromycin	Voriconazole	
	Nefazodone	Ketoconazole	
	Cobicistat	Itraconazole	
	Saquinavir	Posaconazole	
	Ritonavir	Gemfibrozil	
	Nelfinavir	Clopidogrel	
	Indinavir		

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Erleada Prescribing Information, Feb. 2018, Janssen Products.

16. Apalutamide / Therapeutic Effectiveness _____ _____

Alert Message: The safety and effectiveness of Erleada (apalutamide) in pediatric patients have not been established.

Conflict Code: TA - Therapeutic Effectiveness
Drugs/Diseases

Util A	Util B	Util C
Apalutamide		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Erleada Prescribing Information, Feb. 2018, Janssen Products.

17. Apalutamide / Nonadherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Erleada (apalutamide). Non-adherence to the prescribed dosing regimen may result in subtherapeutic effects, which may lead to decreased patient outcomes and additional medical cost.

Conflict Code: LR - Nonadherence
Drugs/Diseases

Util A	Util B	Util C
Apalutamide		

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005; 353:487- 497.
Greer JA, Amoyal N, Nisotel L, et al. Systemic Review of Adherence to Oral Antineoplastic Therapies. The Oncologist. 2016;21:354-376.

18. Apalutamide / P-gp, BCRP or OATP1B1 Substrates _____ _____

Alert Message: Erleada (apalutamide) was shown to be a weak inducer of P-glycoprotein (P-gp), breast cancer resistance protein (BCRP), and organic anion transporting polypeptide 1B1 (OATP1B1) clinically. Concomitant use of apalutamide with medications that are substrates of P-gp, BCRP, or OATP1B1 can result in lower exposure of these medications. Use caution if substrates of P-gp, BCRP, or OATP1B1 must be co-administered with apalutamide and evaluate for loss of activity if medication is continued.

Conflict Code: DD – Drug/ Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Apalutamide	Sulfasalazine	
	Dabigatran	
	Digoxin	
	Fexofenadine	
	Pibrentasvir	
	Sofosbuvir	
	Pravastatin	
	Prazosin	
	Chlorothiazide	
	Methotrexate	
	Topotecan	
	Dantrolene	
	Cimetidine	
	Nitrofurantoin	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Erleada Prescribing Information, Feb. 2018, Janssen Products.

19. Apalutamide / Substrates of CYP 3A4, 2C19, and 2C9 _____ _____

Alert Message: Erleada (apalutamide) is a strong inducer of CYP3A4 and CYP2C19, and a weak inducer of CYP2C9 in humans. Concomitant use of apalutamide with medications that are primarily metabolized by CYP3A4, CYP2C19, or CYP2C9 can result in lower exposure to these medications. Substitution for these medications is recommended when possible or evaluate for loss of activity if medication is continued.

Conflict Code: DD – Drug/ Drug Interaction
Drugs/Diseases

Util A	Util B				
Apalutamide	Amiodarone	Buprenorphine	Budesonide	Etoposide	Dexamethasone
	Fentanyl	Cabozantinib	Buspirone	Estrogens	Dexlansoprazole
	Omeprazole	Midazolam	Disopyramide	Cariprazine	Copanlisib
	Quinidine	Warfarin	Abemaciclib	Amlodipine	Ceritinib
	Crizotinib	Diazepam	Lansoprazole	Acalabrutinib	Atazanavir
	Chlordiazepoxide	Dabrafenib	Diltiazem	Rabeprazole	Oxycodone
	Bedaquiline	Cilostazol	Saxagliptin	Rilpivirine	Celecoxib
	Hydrocodone	Bortezomib	Etravirine	Dapsone	Lovastatin
	Glimepiride	Carbamazepine	Bosutinib	Citalopram	Darifenacin
	Duvelisib	Phenytoin	Lansoprazole	Brexpiprazole	Clarithromycin
	Darunavir	Efavirenz	Fluticasone	Brigatinib	Clonazepam
	Dasatinib	Elbasvir	Brentuximab	Bromocriptine	Clorazepate
	Eletriptan	Everolimus	Felodipine	Encorafenib	Eplerenone
	Erlotinib	Estazolam	Estradiol	Eszopiclone	Ethosuximide
	Etoposide	Flurazepam	Fosamprenavir	Gefitinib	Glasdegib
	Guanfacine	Haloperidol	Idelalisib	Imatinib	Isradipine
	Ixabepilone	Lapatinib	Larotrectinib	Levomilnacipran	Macitentan
	Maraviroc	Mefloquine	Repaglinide	Midostaurin	Mifepristone
	Mirtazapine	Nelfinavir	Torsemide	Nevirapine	Nifedipine
	Nilotinib	Nisoldipine	Ospemifene	Paclitaxel	Palbociclib
	Panobinostat	Pazopanib	Pimavanserin	Vilazodone	Zolpidem
	Quetiapine	Ranolazine	Regorafenib	Ribociclib	Rifabutin
	Roflumilast	Romidepsin	Ruxolitinib	Saquinavir	Sildenafil
	Silodosin	Solifenacin	Sunitinib	Suvorexant	Tadalafil
	Tasimelteon	Temsirolimus	Ticagrelor	Tipranavir	Tolterodine
	Toremifene	Trabectedin	Trazodone	Triazolam	Valbenazine
	Verapamil	Vardenafil	Vemurafenib	Venlafaxine	
	Vinblastine	Vincristine	Vinorelbine	Vorapaxar	
	Avatrombopag	Carvedilol	Simvastatin	Dronabinol	
	Glyburide	Nateglinide	Ospemifene	Terbinafine	
	Valproic Acid	Bictegravir	Pantoprazole	Atorvastatin	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Erleada Prescribing Information, Feb. 2018, Janssen Products.

20. Apalutamide / UGT Substrates _____ _____

Alert Message: Concomitant administration of Erleada (apalutamide) with medications that are substrates of UDP-glucuronosyl transferase (UGT) can result in decreased substrate exposure. Use caution if substrates of UGT must be co-administered with apalutamide and evaluate for loss of activity.

Conflict Code: DD – Drug/ Drug Interaction
Drugs/Diseases

Util A	Util B			
Apalutamide	Canagliflozin	Deferasirox	Indacaterol	Irinotecan
	Imipramine	Acetaminophen	Vorinostat	Pitavastatin
	Lamotrigine	Lorazepam	Olanzapine	
	Mycophenolate	Raloxifene	Oxazepam	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Erleada Prescribing Information, Feb. 2018, Janssen Products.
Knights KM, Rowland A, Miners JO. Renal Drug Metabolism in Humans: The Potential for Drug-Endobiotic Interaction involving P-450 (CYP) and UDP-Glucuronosyltransferase (UGT). Br J Clin Pharmacol. 2013 Oct;76(4):587-602.

21. Apalutamide / Therapeutic Appropriateness _____ _____

Alert Message: Based on the mechanism of action and findings in an animal reproduction study, advise male patients with female partners of reproductive potential to use effective contraception during treatment and for 3 months after the last dose of Erleada (apalutamide).

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Apalutamide		

Gender: Male

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Erleada Prescribing Information, Feb. 2018, Janssen Products.

22. Galcanezumab-gnlm / Overutilization _____ _____

Alert Message: Emgality (galcanezumab-gnlm) may be over-utilized. The recommended dosage of galcanezumab-gnlm is 240 mg once as a loading dose, followed by doses of 120 mg injected subcutaneously once monthly.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C
Galcanezumab-gnlm		

Max Dose:1 pen per month after loading dose

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Emgality Prescribing Information, September 2018, Eli Lilly and Company.

Criteria Recommendations *Approved* *Rejected*

23. Galcanezumab-gnlm / Therapeutic Appropriateness (0 – 17 yoa) _____ _____
Alert Message: The safety and effectiveness of Emgality (galcanezumab-gnlm) in pediatric patients have not been established.

Conflict Code: TA - Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Galcanezumab-gnlm		

Age Range: 0 - 17 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Emgality Prescribing Information, September 2018, Eli Lilly and Company.

24. Galcanezumab-gnlm / Lactation _____ _____
Alert Message: There are no data on the presence of Emgality (galcanezumab-gnlm) in human milk, the effects on the breastfed infant, or the effects on milk production. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for galcanezumab-gnlm and any potential adverse effects on the breastfed infant from galcanezumab-gnlm or from the underlying maternal condition.

Conflict Code: MC – Drug (actual) Disease Precaution
Drugs/Diseases

Util A	Util B	Util C
Galcanezumab-gnlm	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Emgality Prescribing Information, September 2018, Eli Lilly and Company.

25. Galcanezumab-gnlm / Nonadherence _____ _____
Alert Message: Based on refill history, your patient may be underutilizing Emgality (galcanezumab-gnlm). Nonadherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.

Conflict Code: LR Nonadherence
Drugs/Diseases

Util A	Util B	Util C
Galcanezumab-gnlm		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med. 2005; 353(5):487–497.
Emgality Prescribing Information, September 2018, Eli Lilly and Company.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

26. Symtuza / Overutilization _____ _____

Alert Message: The manufacturer's recommended dose of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) is one tablet taken orally once daily.

Conflict Code: ER - Overutilization

Drugs/Diseases		
Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide		

Max Dose: 1 tablet/day

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

27. Symtuza / Severe Renal Impairment _____ _____

Alert Message: Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) is not recommended for use in patients with severe renal impairment (creatinine clearance below 30 mL per minute).

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases		
Util A	Util B	Util C **(Include)**
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide		CKD 4 CKD 5 ESRD

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

28. Symtuza / Severe Hepatic Impairment _____ _____

Alert Message: Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) is not for use in patients with severe hepatic impairment (Child-Pugh Class C). This fixed dose combination antiretroviral agent has not been studied in patients with severe hepatic impairment, and there are only limited data regarding the use of the individual components in patients with severe hepatic impairment.

Conflict Code: TA – Therapeutic Appropriateness

Drugs/Diseases		
Util A	Util B	Util C **(Include)**
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide		Cirrhosis Hepatic Failure

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

29. Symtuza / Contraindicated Drugs _____ _____

Alert Message: A review of recent pharmacy claims shows that the patient is receiving concurrent therapy with Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) and a drug that is contraindicated with the fixed-dose combination agent. Concurrent use of Symtuza with the identified drug may result in serious and/or life-threatening events.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Alfuzosin	Elbasvir/Grazoprevir	
	Ranolazine	Lovastatin	
	Dronedarone	Simvastatin	
	Carbamazepine	Revatio	
	Phenobarbital	Midazolam	
	Phenytoin	Triazolam	
	Rifampin	Dihydroergotamine	
	Lurasidone	Ergotamine	
	Pimozide	Methylergonovine	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

30. Symtuza / Colchicine / Hepatic & Renal Impairment _____ _____

Alert Message: Coadministration of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with colchicine is contraindicated in patients with renal and/or hepatic impairment due to the potential for serious and/or life-threatening reactions.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Colchicine	Renal Impairment
		Hepatic Impairment

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

31. Symtuza / Colchicine / Hepatic & Renal Impairment Negating _____ _____

Alert Message: Coadministration of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with colchicine may increase colchicine plasma concentrations, and dosage adjustment of colchicine is required. Please refer to the official prescribing Information for the recommended dosage adjustments. The concurrent use of Symtuza with colchicine in patients with renal or hepatic impairment is contraindicated.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Colchicine	Renal Impairment
		Hepatic Impairment

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard

32. Symtuza / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) in pediatric patients less than 18 years of age have not been established. Darunavir, a component of the combination antiretroviral product, is not recommended in pediatric patients below the age of 3 years of age because of toxicity and mortality in juvenile rats dosed with darunavir.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide		

Age Range: 0 – 17 yoa

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.

33. Symtuza / Pregnancy / Pregnancy Negating _____ _____

Alert Message: Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) is not recommended for use during pregnancy because of substantially lower exposures of darunavir and cobicistat during pregnancy. Symtuza should not use initiated in pregnant individuals. An alternative regimen is recommended for individuals who become pregnant during therapy with Symtuza.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Pregnancy	Miscarriage Delivery Abortion

Age Range: 11 - 50
Gender: Female

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard

34. Symtuza / All Other Antiretrovirals _____ _____

Alert Message: Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) is a complete regimen for the treatment of HIV-1 infection and coadministration with other antiretroviral medications is not recommended.

Conflict Code: TA – Therapeutic Appropriateness
Drugs/Diseases

Util A	Util B
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Cellular Chemokine Receptor (CCR5) Antagonist Fusion Inhibitors Integrase Inhibitors NNRTIs NRTIs Nucleotide Analog Reverse Transcriptase Inhibitors Protease Inhibitors Other Antiretroviral Combos

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard

35. Symtuza / Nonadherence _____ _____

Alert Message: Based on the refill history, your patient may be under-utilizing Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide). Nonadherence to antiretroviral therapy may result in insufficient plasma levels and partial suppression of viral load leading to the development of resistance, HIV progression, and increased mortality.

Conflict Code: LR - Nonadherence
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide		

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the Use of Antiretroviral Agents in HIV-1 Infected Adults and Adolescents. Department of Health and Human Services. May 30, 2018.
Available at: http://www.aidsinfo.nih.gov/guidelines/ht,l/1/adult-and-adolescent-arv/0
Hoffman C, Mulcahy F, Goals and Principles of Therapy - Eradication, Cost, Prevention and Adherence. Hoffman C, Rockstroh J, Kamps BS, eds. HIV Medicine, Flying Publishers-Paris, Cagliari, Wuppertal, Sevilla, 2005:167-173.

36. Symtuza / Antiarrhythmic Agents that are CYP3A4 Substrates _____ _____

Alert Message: Caution should be exercised when administering Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with antiarrhythmic drugs that are CYP3A4 and/or CYP2D6 substrates. Concurrent use of these agents may result in an increase in the antiarrhythmic plasma concentrations due to inhibition of CYP3A4- and/or CYP2D6-mediated metabolism by the darunavir and cobicistat components of the antiretroviral agent. Clinical monitoring is recommended upon coadministration with these antiarrhythmics.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Amiodarone Disopyramide Flecainide Propafenone Quinidine Mexiletine	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard

37. Symtuza / Digoxin _____ _____

Alert Message: Caution should be exercised when administering Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with digoxin, a P-gp substrate. Concurrent use of these agents may result in an increase in digoxin plasma concentrations due to inhibition of P-gp-mediated transport by the cobicistat component of the antiretroviral.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Digoxin	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

38. Symtuza / Clarithromycin & Erythromycin _____ _____

Alert Message: Caution should be exercised when administering Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with clarithromycin or erythromycin. Concurrent use of these agents may result in an increase in the plasma concentrations of the antibacterial as well as the darunavir and cobicistat components of the antiretroviral. The antibacterial and antiretroviral agents are both CYP3A4 substrates and inhibitors. Consider alternative antibiotic therapy with concomitant use of Symtuza.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Clarithromycin Erythromycin	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

39. Symtuza / Dasatinib _____ _____

Alert Message: Caution should be exercised when administering Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with dasatinib. Concurrent use of these agents may result in an increase in dasatinib plasma concentrations due to the inhibition of dasatinib CYP3A4-mediated metabolism by the cobicistat and darunavir components of the antiretroviral. A decrease in the dasatinib dosage may be necessary. Consult the official prescribing Information for dasatinib for the recommended dosage adjustment.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Dasatinib	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.

40. Symtuza / Eslicarbazepine & Oxcarbazepine _____ _____

Alert Message: The concurrent use of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with eslicarbazepine or oxcarbazepine may cause a significant decrease in the plasma concentrations or the darunavir and cobicistat components of the combination antiretroviral agent, leading to the potential loss of virologic efficacy and development of resistance. Consider alternative anticonvulsant or antiretroviral therapy to avoid changes in exposure. If coadministration is necessary, monitor the patient for lack of virologic response.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Eslicarbazepine Oxcarbazepine	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.

41. Symtuza / Clonazepam _____ _____

Alert Message: Caution should be exercised when coadministering Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with clonazepam. Concurrent use of these agents may result in an increase in clonazepam plasma concentrations due to inhibition of clonazepam CYP3A4-mediated metabolism by the darunavir and cobicistat components of the antiretroviral. Clinical monitoring of clonazepam is recommended when these agents are coadministered.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Clonazepam	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

42. Symtuza / SSRIs, TCAs & Trazodone _____ _____

Alert Message: Caution should be exercised when coadministering Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with a selective serotonin reuptake inhibitor, tricyclic antidepressant, or trazodone. The cobicistat component of the antiretroviral agent is a CYP3A4 and CYP2D6 inhibitor, and concurrent use with drugs that are CYP3A4 and CYP2D6 substrates may result in elevated substrate plasma concentrations. Careful dose titration of the antidepressant and monitoring for response are recommended.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	SSRIs TCAs Trazodone	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

43. Symtuza / Ketoconazole & Itraconazole _____ _____

Alert Message: Coadministration of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with ketoconazole or itraconazole may result in increased plasma concentrations of the antifungal as well as the plasma concentrations of the antiretroviral components, darunavir and cobicistat. Darunavir, cobicistat, and both of the antifungals are CYP3A4 substrates and inhibitors. Monitor the patient for increased antifungal and antiretroviral-related adverse effect.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Ketoconazole Itraconazole	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

44. Symtuza / Voriconazole _____ _____

Alert Message: Concurrent use of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with voriconazole is not recommended unless the benefit/risk assessment justifies the use of voriconazole. Voriconazole and the antiretroviral components, darunavir and cobicistat, are CYP3A4 substrates and inhibitors. The effects of concurrent use if unknown.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Voriconazole	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

45. Rifabutin / Symtuza _____ _____

Alert Message: The concurrent use of Symtuza darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with rifabutin is not recommended. If the combination is warranted, the recommended dose of rifabutin is 150 mg every other day. Coadministration may result in increased rifabutin plasma concentrations and decreased tenofovir plasma concentrations. Monitor the patient for rifabutin-related adverse reactions including neutropenia and uveitis.

Conflict Code: ER - Overutilization
Drugs/Diseases

Util A	Util B	Util C **(Include)**
Rifabutin		Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide

Max Dose: 1 capsule every other day

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

46. Symtuza / Rifapentine _____ _____

Alert Message: The concurrent use of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with rifapentine is not recommended due to the potential for loss of virologic efficacy and development of resistance to the antiretroviral agent. The darunavir and tenofovir components of the antiretroviral combination product are CYP3A4 substrates, and coadministration with rifapentine, a CYP3A4 inducer, can result in decreased plasma concentrations of both tenofovir and darunavir.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Rifapentine	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

47. Symtuza / Antipsychotics Metabolized by 3A4 or 2D6 _____ _____

Alert Message: Coadministration of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with an antipsychotic agent that is metabolized by CYP3A4 or CYP2D6 may result in increased plasma concentrations of the antipsychotic. The darunavir and cobicistat components of the combination antiretroviral agent are CYP3A4 and CYP2D6 inhibitors. Dose reduction of the antipsychotic may be needed when coadministered with Symtuza.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Perphenazine	Pimavanserin	
	Risperidone	Lurasidone	
	Thioridazine	Aripiprazole	
	Quetiapine	Brexpiprazole	
	Chlorpromazine	Cariprazine	
	Fluphenazine	Iloperidol	
	Haloperidol	Clozapine	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

48. Symtuza / Beta-Blockers Metabolized by 2D6 _____ _____

Alert Message: Coadministration of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with a beta-blocker that is metabolized by CYP2D6 may result in increased plasma concentrations of the beta-blocker. The darunavir and cobicistat components of the combination antiretroviral agent are CYP2D6 inhibitors. Clinical monitoring for signs of increased pharmacologic and adverse effects of the beta-blocker is recommended.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Carvedilol	
	Metoprolol	
	Propranolol	
	Timolol	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

49. Symtuza / Calcium Channel Blockers Metabolized by 3A4 _____ _____

Alert Message: Coadministration of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with a calcium channel blocker (CCB) that is metabolized by CYP3A4 may result in increased plasma concentrations or the calcium channel blocker. The darunavir and cobicistat components of the combination antiretroviral agent are CYP3A4 inhibitors. Clinical monitoring for signs of increased pharmacologic and adverse effects of the CCB is recommended.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B		Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Amlodipine	Nicardipine	
	Diltiazem	Nimodipine	
	Felodipine	Nisoldipine	
	Verapamil	Nifedipine	
	Isradipine		

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

50. Symtuza / Atorvastatin 40 & 80 mg _____ _____

Alert Message: The dosage of atorvastatin should not exceed 20 mg/day in patients receiving concurrent therapy with Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide). Cobicistat and darunavir are both CYP3A4 inhibitors and concurrent use with atorvastatin, a CYP3A4 substrate, may result in increased atorvastatin plasma concentrations and increased risk for atorvastatin-related adverse reactions (e.g., myopathy and rhabdomyolysis).

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Atorvastatin 40 & 80 mg	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

51. Symtuza / Rosuvastatin 20 & 40 mg _____ _____

Alert Message: The dosage of rosuvastatin should not exceed 10 mg/day in patients receiving concurrent therapy with Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide). Cobicistat is an OATP1B1 transport inhibitor and concurrent use with rosuvastatin, an OATP1B1 substrate, may result in increased rosuvastatin plasma concentrations and increased risk of rosuvastatin-related adverse reactions (e.g., myopathy and rhabdomyolysis).

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Rosuvastatin 20 & 40 mg	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

52. Symtuza / Dexamethasone _____ _____

Alert Message: The concurrent use of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide with dexamethasone may result in decreased plasma concentrations of the cobicistat and darunavir components of the combo antiretroviral which may result in loss of antiretroviral efficacy and the potential development of viral resistance. Darunavir and cobicistat are CYP3A4 substrates and dexamethasone is a CYP3A4 inducer. Dexamethasone concentrations may be increased. Alternative corticosteroid therapy should be considered for patients prescribed Symtuza.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Dexamethasone	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

53. Symtuza / Methylprednisolone _____ _____

Alert Message: The concurrent use of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide with methylprednisolone may result in increased methylprednisolone plasma concentrations and the potential for Cushing's syndrome and adrenal suppression. Darunavir and cobicistat are CYP3A4 inhibitors and methylprednisolone is a CYP3A4 substrate. Alternative corticosteroids whose concentrations are less affected by CYP3A4 inhibitors should be considered, especially for long-term use.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Methylprednisolone	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

54. Symtuza / Prednisone _____ _____

Alert Message: The concurrent use of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with prednisone may result in increased prednisone plasma concentrations and the potential for Cushing's syndrome and adrenal suppression. Darunavir and cobicistat are CYP3A4 inhibitors and prednisone is a CYP3A4 substrate. Alternative corticosteroids whose concentrations are less affected by CYP3A4 inhibitors should be considered, especially for long-term use.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Prednisone	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

55. Symtuza / Fluticasone _____ _____

Alert Message: The concurrent use of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with a fluticasone-containing product may result in increased fluticasone plasma concentrations due to inhibition of fluticasone CYP3A4-mediated metabolism by the cobicistat and darunavir components of the antiretroviral product. Concomitant therapy may result in adverse systemic corticosteroid effects.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Fluticasone	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

56. Symtuza / Mometasone _____ _____

Alert Message: The concurrent use of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with mometasone may result in increased mometasone plasma concentrations due to inhibition of mometasone CYP3A4-medicated metabolism by the cobicistat and darunavir components of the antiretroviral product. Concomitant therapy may result in adverse systemic corticosteroid effects. Alternative corticosteroids should be considered, particularly for long-term use.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Mometasone	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

57. Symtuza / CYP3A4 Metabolized Sedatives _____ _____

Alert Message: Coadministration of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with a sedative/hypnotic that is metabolized by CYP3A4 may result in increased plasma concentrations of the sedative/hypnotic. The darunavir and cobicistat components of the combination antiretroviral agent are CYP3A4 inhibitors. Dose reduction and clinical monitoring of the sedative/hypnotic agent should be considered when coadministered with Symtuza.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Buspirone Diazepam Estazolam Zolpidem Flurazepam Chlordiazepoxide Clorazepate	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

58. Symtuza / Salmeterol _____ _____

Alert Message: Coadministration of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with a salmeterol-containing agent is not recommended. Concurrent use may result in increased risk of cardiovascular adverse events associated with salmeterol, including QT prolongation, palpitations, and sinus tachycardia.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Salmeterol	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

59. Symtuza / Bosentan _____ _____

Alert Message: The concurrent use of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with Tracleer (bosentan) may result in increased plasma concentrations of bosentan and decreased plasma concentrations of cobicistat and darunavir. All three agents are CYP3A4 substrates while bosentan is a potent CYP3A4 inducer and cobicistat and darunavir are CYP3A inhibitors. Refer to the official cobicistat prescribing Information for the appropriate dosing upon initiation of concomitant therapy with these agents.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Bosentan	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

60. Symtuza / Everolimus _____ _____

Alert Message: Coadministration of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with everolimus (a CYP3A4 and P-gp substrate) is not recommended. The cobicistat and darunavir components of the antiretroviral agent are strong inhibitors of CYP3A4 and also inhibit P-gp transport. Concurrent use of these drugs may result in a significant increase in everolimus plasma concentrations.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Everolimus	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

61. Symtuza / CYP3A4 Metabolized Immunosuppressants _____ _____

Alert Message: Caution should be exercised when coadministering Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with an immunosuppressant that is a CYP3A4 substrate. The cobicistat and darunavir components of the antiretroviral agent are inhibitors of CYP3A4, and concurrent use of these agents may result in increased immunosuppressant plasma concentrations. Therapeutic drug monitoring is recommended with concomitant use.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Cyclosporine Sirolimus Tacrolimus	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

62. Symtuza / Tramadol _____ _____

Alert Message: The concurrent use of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with a tramadol-containing agent may result in increased plasma concentrations of the parent drug tramadol and decreased levels of the active metabolite of tramadol. A dose decrease for tramadol may be needed when these agents are coadministered. Tramadol is a CPY3A4 and CYP2D6 substrate, and the cobicistat and darunavir components of the antiretroviral agent inhibit both CYP3A4- and CYP2D6-mediated metabolism.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Tramadol	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

63. Symtuza / Avanafil _____ _____

Alert Message: The concurrent use of Stendra (avanafil) with Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) is not recommended because a safe and effective avanafil dosage regimen has not been established. Consider an alternative PDE-5 inhibitor that has dosing recommendations established and provided in the official prescribing Information.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Avanafil	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

64. Symtuza / Buprenorphine _____ _____

Alert Message: The concurrent use of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with a buprenorphine-containing agent may result in increased buprenorphine plasma concentrations. Buprenorphine is a CYP3A4 substrate, and the cobicistat and darunavir components of the antiretroviral agent inhibit CYP3A4-mediated metabolism. If buprenorphine is initiated in a patient taking Symtuza, titrate the buprenorphine dose to the desired effect. If Symtuza is initiated in a patient taking buprenorphine, a dose adjustment of buprenorphine may be needed.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Buprenorphine	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

65. Symtuza / Drospirenone/Ethinyl Estradiol _____ _____

Alert Message: The concurrent use of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with a drospirenone-containing agent may result in increased drospirenone plasma concentrations, putting the patients at risk of drospirenone-related adverse effects (e.g., hyperkalemia). Clinical monitoring is recommended when these agents are coadministered.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Drospirenone	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

66. Symtuza / Estrogen-based Contraceptives _____ _____

Alert Message: The concurrent use of Symtuza (darunavir/cobicistat/emtricitabine/tenofovir alafenamide) with estrogen-based contraceptives may result in decreased pharmacologic effects of the contraceptive agent. Additional or alternative (non-hormonal) forms of contraception should be considered in these patients.

Conflict Code: DD – Drug/Drug Interaction
Drugs/Diseases

Util A	Util B	Util C
Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide	Estrogen-Based Contraceptives	

References:
Symtuza Prescribing Information, Feb. 2019, Janssen Products, LP.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

67. Erenumab-aooe / Overutilization _____ _____

Alert Message: Aimovig (erenumab-aooe) may be over-utilized. The recommended dosage of erenumab-aooe is 70 mg injected subcutaneously once monthly. Some patients may benefit from a dosage of 140 mg injected subcutaneously once monthly, which is administered as two consecutive subcutaneous injections of 70 mg each.

Drugs/Diseases

Util A	Util B	Util C
Erenumab-aooe		

Max Dose: 2 pens per month

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Aimovig Prescribing Information, May 2018, Amgen Inc.

68. Erenumab-aooe / Therapeutic Appropriateness (0 – 17 yoa) _____ _____

Alert Message: The safety and effectiveness of Aimovig (erenumab-aooe) in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Erenumab-aooe		

Age Range: 0 - 17 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Aimovig Prescribing Information, May 2018, Amgen Inc.

69. Erenumab-aooe / Lactation _____ _____

Alert Message: There are no data on the presence of Aimovig (erenumab-aooe) in human milk, the effects on the breastfed infant, or the effects on milk production. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for erenumab-aooe and any potential adverse effects on the breastfed infant from erenumab-aooe or from the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Erenumab-aooe	Lactation	

Gender: Female
Age Range: 11 – 50 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Aimovig Prescribing Information, May 2018, Amgen Inc.

70. Erenumab-aooe / Nonadherence _____ _____

Alert Message: Based on refill history, your patient may be underutilizing Aimovig (erenumab-aooe). Nonadherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.

Drugs/Diseases

Util A	Util B	Util C
Erenumab-aooe		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med. 2005; 353(5):487–497.
Aimovig Prescribing Information, May 2018, Amgen Inc.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

71. Pimavanserin / Nonadherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Nuplazid (pimavanserin). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.

Conflict Code: LR - Nonadherence
Drugs/Diseases

Util A	Util B	Util C
Pimavanserin		

References:
Osterberg L, Blaschke T. Adherence to Medication. N Engl J Med 2005;353:487-97.
Stephenson JJ, Tuncelli O, Gu T, et al., Adherence to Oral Second-Generation Antipsychotic Medications in Patients with Schizophrenia and Bipolar Disorder: Physicians' Perceptions of Adherence vs. Pharmacy Claims. Int J Clin Pract, June 2012, 66, 6, 565-573.
Fleisher JE, Stern MB. Medication Non-adherence in Parkinson's Disease. Curr Neurol Neurosci Rep. 2013;13(10):382. doi 10 01007/s11910-013-0382-z

72. Ibalizumab-uiyk / Nonadherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Trogarzo (ibalizumab-uiyk). Nonadherence to the antiretroviral therapy may result in insufficient plasma levels and partial suppression of viral load leading to the development of resistance, HIV progression, and increased mortality.

Drugs/Diseases

Util A	Util B	Util C
Ibalizumab-uiyk		

References:
Trogarzo Prescribing Information, May 2018, Theratechnologies, Inc.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

73. Ibalizumab-uiyk / Therapeutic Appropriateness _____ _____

Alert Message: A review of recent pharmacy claims reveals that the patient is not receiving an optimal background regimen (OBR) of antiretroviral medications in addition to Trogarzo (ibalizumab-uiyk). Ibalizumab-uiyk is FDA approved to be used in combination with other antiretroviral agents for the treatment of HIV-1 infection.

Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Ibalizumab-uiyk		Antiretrovirals

References:
Trogarzo Prescribing Information, May 2018, Theratechnologies, Inc.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

74. Ibalizumab-uiyk / Therapeutic Appropriateness _____ _____

Alert Message: The safety and effectiveness of Trogarzo (ibalizumab-uiyk) in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Ibalizumab-uiyk		

Age Range: 0 – 17 yoa

References:
Trogarzo Prescribing Information, May 2018, Theratechnologies, Inc.
Clinical Pharmacology, 2019 Elsevier/Gold Standard.

75. Amantadine ER / Overutilization _____ _____

Alert Message: The manufacturer's recommended maximum daily dose of Osmolex ER (amantadine extended-release) is 322 mg, taken in the morning.

Drugs/Diseases

Util A	Util B	Util C **(Negating)**
Amantadine ER		CKD 3, 4, & 5
		ESRD

Max Dose: 322 mg/day

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Osmolex ER Prescribing Information, Feb. 2018, Vertical Pharmaceuticals, LLC.

76. Amantadine ER / Overutilization Moderate Renal Impairment _____ _____

Alert Message: The manufacturer's recommended maximum daily dose of Osmolex ER (amantadine extended-release) in patients with moderate renal impairment (CrCl 30 - 59 mL/min/1.73m2) is 322 mg once every 48 hours.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Amantadine ER		CKD 3

Max Dose: 322 mg/48 hrs

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Osmolex ER Prescribing Information, Feb. 2018, Vertical Pharmaceuticals, LLC.

77. Amantadine ER / Overutilization Severe Renal Impairment _____ _____

Alert Message: The manufacturer's recommended maximum daily dose of Osmolex ER (amantadine extended-release) in patients with severe renal impairment (CrCl 15 - 29 mL/min/1.73m2) is 322 mg every 96 hours.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Amantadine ER		CKD 4 & 5

Max Dose: 68.5 mg/day

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Osmolex ER Prescribing Information, Feb. 2018, Vertical Pharmaceuticals, LLC.

78. Amantadine ER / End Stage Renal Disease _____ _____

Alert Message: The use of Osmolex ER (amantadine extended-release) in patients with end-stage renal disease (CrCl < 15 mL/min/1.73m2) is contraindicated. The clearance of amantadine is significantly reduced in patients with renal insufficiency.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Amantadine ER		ESRD

References:
Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Osmolex ER Prescribing Information, Feb. 2018, Vertical Pharmaceuticals, LLC.

79. Revefenacin / Overutilization _____ _____

Alert Message: The recommended dose of Yupelri (revefenacin) inhalation solution is one 175 mcg unit-dose vial administered once daily by nebulizer using a mouthpiece.

Drugs/Diseases

Util A	Util B	Util C
Revefenacin		

Max Dose: 1 inhalation/day

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

80. Revefenacin / Glaucoma _____ _____

Alert Message: Yupelri (revefenacin) should be used with caution in patients with narrow-angle glaucoma. Revefenacin is a long-acting muscarinic antagonist, and its use in this patient population can worsen the condition.

Drugs/Diseases

Util A	Util B	Util C (Include)
Revefenacin		Glaucoma

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

81. Revefenacin / Urinary Retention, Prost Hyperplasia & Bladder Neck Obs _____ _____

Alert Message: Yupelri (revefenacin) should be used with caution in patients with urinary retention. Prescribers and patients should be alert for signs and symptoms of urinary retention (e.g., difficulty passing urine, painful urination), especially in patients with prostatic hyperplasia or bladder-neck obstruction. Instruct patients to consult a healthcare provider immediately if any of these signs or symptoms develop.

Drugs/Diseases

Util A	Util B	Util C
Revefenacin	Urinary Retention Prostatic Hyperplasia Bladder-Neck Obstruction	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

82. Revefenacin / Anticholinergics _____ _____

Alert Message: The concurrent use of Yupelri (revefenacin) with anticholinergic agents should be avoided. Revefenacin is a long-acting muscarinic antagonist, and co-administration with anticholinergics may lead to an increase in anticholinergic adverse effects.

Drugs/Diseases

Util A	Util B				Util C
Revefenacin	Trihexyphenidyl	Trospium	Cyclizine	Oxybutynin	
	Benztropine	Hyoscyamine	Dicyclomine	Trimethobenzamide	
	Orphenadrine	Scopolamine	Diphenhydramine	Flavoxate	
	Darifenacin	Propantheline	Meclizine	Metscopolamine	
	Fesoterodine	Mepenzolate	Solifenacin	Tolterodine	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

83. Revefenacin / OATP1B1 & OATP1B3 Inhibitors _____ _____

Alert Message: The concurrent use of Yupelri (revefenacin) with OATP1B1 and OATP1B3 inhibitors is not recommended. The active metabolite of revefenacin is a substrate or OATP1B1 and OATP1B3. Coadministration of revefenacin with an inhibitor of these uptake transporters can result in increased systemic exposure to the active metabolite.

Drugs/Diseases

Util A	Util B	Util C
Revefenacin	Rifampicin	Letermovir
	Cyclosporine	Lopinavir
	Clarithromycin	Obeticholic Acid
	Atazanavir	Paritaprevir/Ombitasvir/Ritonavir
	Cobicistat	Rifampin
	Daclatasvir	Velpatasvir/Sofosbuvir/Voxilaprevir
	Eltrombopag	Velpatasvir/Sofosbuvir
	Erythromycin	Teriflunomide
	Gemfibrozil	
	Glecaprevir/Pibrentasvir	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

84. Revefenacin / Therapeutic Appropriateness _____ _____

Alert Message: The safety and efficacy of Yupelri (revefenacin) in pediatric patients have not been established.

Drugs/Diseases

Util A	Util B	Util C
Revefenacin		

Age Range: 0 – 17 yoa

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

85. Revefenacin / Hepatic Impairment _____ _____

Alert Message: Yupelri (revefenacin) is not recommended for use in patients with any degree of hepatic impairment. In a pharmacokinetic study, the systemic exposure of revefenacin was unchanged while that of its active metabolite was increased in subjects with moderate hepatic impairment. The safety of revefenacin has not been evaluated in COPD patients with mild-to-severe hepatic impairment.

Drugs/Diseases

Util A	Util B	Util C **(Include)**
Revefenacin		Hepatic Impairment

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

86. Revefenacin / Pregnancy / Pregnancy Negating _____ _____

Alert Message: There are no adequate and well-documented studies with Yupelri (revefenacin) in pregnant women. Women should be advised to contact their physician if they become pregnant while taking revefenacin.

Drugs/Diseases

Util A	Util B	Util C (Negating)
Revefenacin	Pregnancy	Miscarriage
		Delivery
		Abortion

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

87. Revefenacin / Lactation _____ _____

Alert Message: There is no information regarding the presence of Yupelri (revefenacin) in human milk, the effects on the breastfed infant, or the effects on milk production. However, revefenacin was present in the milk of lactating rats following dosing during pregnancy and lactation. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for revefenacin, and any potential adverse effects on the breastfed infant from revefenacin or from the underlying maternal condition.

Drugs/Diseases

Util A	Util B	Util C
Revefenacin	Lactation	

References:
Clinical Pharmacology, 2019 Elsevier/Gold Standard.
Yupelri Prescribing Information, November 2018, Mylan.

88. Revefenacin / Nonadherence _____ _____

Alert Message: Based on refill history, your patient may be under-utilizing Yupelri (revefenacin). Non-adherence to the prescribed dosing regimen may result in sub-therapeutic effects, which may lead to decreased patient outcomes and additional healthcare costs.

Drugs/Diseases

Util A	Util B	Util C
Revefenacin		

References:

van Boven JF, Chavannes NH, van der Molen T, et al. Clinical and Economic Impact of Non-adherence in COPD: A Systematic Review. Respir Med. 2015 Jan;108(1):103-113.
Restrepo RD, Alvarez MT, Wittnebel LD, et al., Medication Adherence Issues in Patients Treated for COPD. International Journal of COPD. 2008;3(3):371-384.
Simoni-Wastila L, Wei Y, Qian J, et al., Association of Chronic Obstructive Pulmonary Disease Maintenance Medication Adherence With All-Cause Hospitalization and Spending in a Medicare Population. Am Jrnl Geriatr Pharmacother. 2012 Jun;10(3):201-210.
Lareau SC, Yawn BP. Improving Adherence with Inhaler Therapy in COPD. International Journal COPD. 2010 Nov 24;5:401-406.

89. Amantadine ER / Alcohol Dependence _____ _____

Alert Message: Concomitant use of Osmolex ER (amantadine extended-release) with alcohol is not recommended, as it may increase the potential for CNS effects such as dizziness, confusion, lightheadedness, and orthostatic hypotension.

Drugs/Diseases

Util A	Util B	Util C
Amantadine ER	Alcohol Dependence	

References:

Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Osmolex ER Prescribing Information, Feb. 2018, Vertical Pharmaceuticals, LLC.

90. Amantadine ER / Drugs Decreasing Urinary pH _____ _____

Alert Message: Concurrent use of Osmolex ER (amantadine extended-release) with a urinary acidifying agent may decrease amantadine serum concentrations due to increased amantadine elimination. The pH of urine influences the excretion rate of amantadine. Monitor the patient for decreased amantadine efficacy.

Drugs/Diseases

Util A	Util B	Util C
Amantadine ER	Methenamine Potassium Phosphate Ascorbic Acid	

References:

Clinical Pharmacology, 2018 Elsevier/Gold Standard.
Osmolex ER Prescribing Information, Feb. 2018, Vertical Pharmaceuticals, LLC.

91. Amantadine ER / Drugs Increasing Urinary pH _____ _____

Alert Message: Concurrent use of Osmolex ER (amantadine extended-release) with a urinary alkalinizing agent may lead to an accumulation of amantadine and risk of amantadine-related adverse effects. The pH of urine influences the excretion rate of amantadine. Alterations of urine pH towards the alkaline condition may lead to accumulation of the drug.

Drugs/Diseases

Util A	Util B		Util C
Amantadine ER	Acetazolamide	Chlorothiazide	
	Dichlorphenamide	Chlorthalidone	
	Methazolamide	Hydrochlorothiazide	
	Potassium Citrate	Methyclothiazide	
	Sodium Citrate	Metolazone	
	Calcium Acetate		
	Sodium Bicarbonate		

References:

Facts & Comparison, 2018 Updates. Wolters Kluwer Health.
Osmolex ER Prescribing Information, Feb. 2018, Vertical Pharmaceuticals, LLC.